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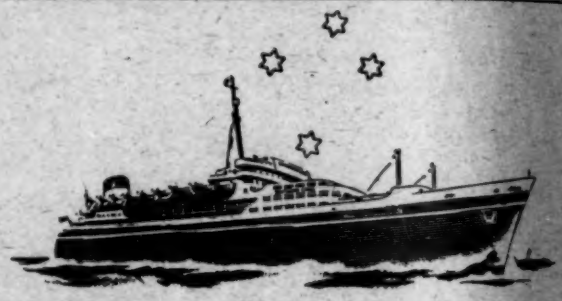

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 26 1955

ENVIRONMENTAL FACTORS IN CERVICAL CANCER

AN APPROACH TO ITS PREVENTION*

BY

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Though preventive measures against disease have long been the basic goal of medical research, their possibility has never been fully appreciated in the field of neoplastic disease. This is true in spite of the fact that such an approach has appeared to be practical since Pott's classical observation on scrotal cancer in chimney-sweeps. In a few instances only, involving primarily industrial cancers, have such measures been advanced. Then recent clinical statistical studies on lung cancer, both historical and prospective, demonstrated that environmental factors play a significant part in the production of this major type of cancer. The results of these surveys have led to a continuation of efforts to search for environmental factors that might influence other types of human cancer.

Our initial environmental cancer studies concentrated on those neoplasms whose incidence data suggested significant differences between population groups. We, furthermore, first investigated epidermoid cancers because these types seem particularly dependent on extrinsic factors. Cancer of the cervix belongs to these groups of cancer. It is predominantly an epidermoid cancer and varies significantly among different population groups. Unless such variations can be accounted for by racial factors, they must be explained by differences in environmental patterns. The present communication serves to summarize the findings which may account for the observed rates of cervical cancer recently reported in greater detail (Wynder *et al.*, 1954).

Rates of Cervical Cancer

For statistically significant variables, which epidemiological cancer studies may reveal, to be regarded also as causatively significant, they must at least in part account for such differences in rates. In Table I are shown the relative rates of cervical cancer which have been reported among different population groups. Not all of the data are available as incidence data. Indian data are available only as frequency rates from Indian hospitals. The following rates are of particular interest:

(*a*) In the United States the incidence of cancer of the cervix among Negroes is 60% higher than among whites, and among the latter it is more common among the lower-income groups (Wynder *et al.*, 1954).

(*b*) The rate of cervical cancer among Jews is only one-fifth to one-tenth of that of the non-Jewish women in the United States, and the difference appears to be even greater if one takes the Jewish rate as observed in Israel (A. Symeonidis, personal communication).

(*c*) A recent report from Denmark by Rojel (1953) shows the rate of cervical cancer among prostitutes to be four times greater than that of non-prostitutes of similar social class.

(*d*) In most Asiatic and South American countries cancer of the cervix is the most common female cancer.

(*e*) Gagnon (1950) found no cancer of the cervix among a large group of nuns studied in Canada. A similar finding was recently shown by Schömig (1953) among German nuns.

(*f*) Cancer of the cervix rarely occurs in women under the age of 20; and in the majority of cases, as reviewed by Pollack and Taylor (1947), before this age, a glandular type of cervical cancer was found.

(*g*) The relative frequency of cancer of the cervix among Hindu women is about 45%, while it is 29% for the Indian Christians, 18% for the Moslems, and 16% for Parsees as based upon extensive records from the Tata Memorial Hospital in Bombay (Khanolkar, 1950).

These incidence and frequency rates of cervical cancer thus show a marked variation. It has been the purpose of this investigation to uncover the reason or reasons for these differences. In Table II are listed the factors which previous investigators have suspected to be associated with the production of cervical cancer.

TABLE I.—*Relative Frequency Rates of Cervical Cancer Among Some Different Population Groups*

Population Group	Relative Rate
Hindus	Very high
Christians (India)	High
Negroes	"
Parsees	Low
Moslems	"
Jews	Very low

TABLE II.—*Factors which Previous Groups of Investigators Have Suspected to be of Significance in the Production of Cancer of the Cervix*

1. Pregnancy and rate of pregnancy
2. Marriage and age of first marriage
3. Cervical laceration
4. Chronic cervicitis
5. Diet
6. Lack of circumcision (poor penile hygiene)
7. Vaginal discharge
8. Hormonal imbalance
9. Coal-tar douching
10. " Racial " factors

*This paper was presented in part before the Annual Meeting of the American Cancer Society, October 18, 1954, New York.

Methodology of Study

The significance of environmental cancer surveys rises and falls with the methodology employed. It is paramount that the study is based upon a representative sample of the types of cancer one wants to study, and it is equally important that a proper comparison group is analysed in identical detail.

The cervical cancer patients were interviewed by specially trained interviewers in nine different hospitals in the United States, with the largest single group being interrogated at the Memorial Center, New York. As controls we selected patients with other pelvic disorders. The control group was age- and hospital-standardized in accord with the cervical cancer group. The analyses were based entirely on epidermoid cancer of the cervix. Microscopical diagnosis was obtained in every case. The Indian cancer cases were interviewed by Dr. P. D. Shroff at the Tata Memorial Hospital in Bombay. The same questionary was used for the American and Indian studies. The questionary attempted to include all of the factors suggested or suspected of playing a part in the development of cervical cancer that could be determined by clinical interrogation.

In part, the interview attempted to obtain information about rather personal matters. It is realized, of course, that not every patient may have told the truth about the age of her first sexual experience. It is also understood that not every patient was certain about the circumcision status of her partner. However, by careful and private interview we have tried to keep such inherent errors to a minimum. Furthermore, the control patients were questioned in the identical manner. It may thus be assumed that some of the inherent interview errors may be balanced out and that actual differences found between the cancer and control groups studied are of real rather than of apparent significance. Upon completion of the interview, the form was edited to assure complete answers to all of the questions, and then the information was coded and punched on special cards. All of the statistical analyses were carried out by Jerome Cornfield, of the Section of Biometry of the National Institutes of Health. Table III shows the number of patients on which this study is based, divided into the respective population groups studied separately.

TABLE III.—*Number of Cervical Cancer and Control Patients Included in Study*

	Cervical Cancer	Controls
U.S.A.:		
White (non-Jewish) ..	354	594
„ (Jewish)	20	326
Negroes	215	391
Total	589	1,311
India:		
Hindu	255	238
Moslem	26	135
Christian	22	80
Parsee	—	62
Total	303	515

If a given variable was found to be significantly different between cancer and control groups, tests were made to determine whether the variable was independently significant or whether it simply depended on some difference in another variable. The pertinent parts of the study are summarized below.

Results

Only along two broad lines did we find significant differences between the cancer and control groups. These referred to the factors of marriage and circumcision. Two negative factors must be stressed because previous investigators had placed much emphasis on these variables. These four factors are discussed in some detail.

Marriage Factor

As in previous studies, we found fewer single women among patients with cancer of the cervix as compared with the controls. Nine per cent. of the controls had never been married, compared with only 2% in the non-Jewish cervix cases. Respective data for the Negro group

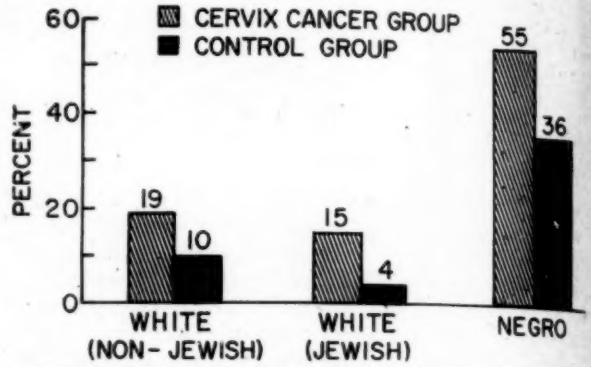

FIG. 1.—Percentage of cervix cancer and control groups in American Hospitals having first coitus at age 16 or before.

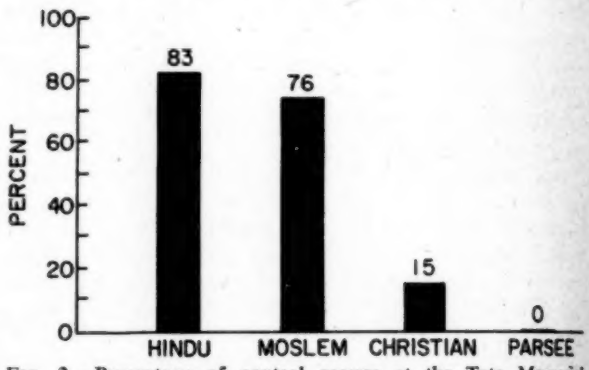

FIG. 2.—Percentage of control groups at the Tata Memorial Hospital in Bombay, India, having first coitus at 16 or before.

were 10% and 4%. The single women were of course further questioned for sexual relationship, and in only three instances out of the total white and Negro cases studied was cervical cancer found in a woman who claimed to be virginal.

Cervical cancer patients were found to marry more frequently than control patients. Of the non-Jewish white patients with cervical cancer, 30% had married more than once, in contrast to 14% of the controls. The respective figures for the Negro group were 35% and 23%.

It was a striking fact that the cervical cancer group married significantly earlier than the control group, as has been previously noted by Lombard and Potter (1950). Marriage at the age of 16 or under, for example, for the white cervical cancer group gave 14%, compared with 8% for the controls. The respective data for the Negro group were 32% and 19%, whereas it was 4% for the Jewish controls. Negroes marry at an earlier age than the non-Jewish whites, who in turn do so earlier than Jewish patients. These data are magnified and certainly of greater importance, though perhaps less reliable, if we note the age of first coitus. For the non-Jewish white cervical cancer group it was 19% before the age of 16 and for the controls 10%. Respective data for the Negroes were 55% and 36%, and for the Jewish group 15% and 4% (Fig. 1).

The Indian data showed a significantly earlier onset of first coitus among Hindus and Moslems as compared with Indian Christians and Parsees (Fig. 2). In India the age of first marriage does not necessarily reflect early intercourse, because of childhood marriages. The age of first coitus data among Hindu controls showed 83% to have had intercourse prior to age 16, whereas 76% of Moslems and only 15% of the Indian Christians, and none of the Parsees interviewed, had sexual relations prior to that age.

The data agree with the concept that those population groups with a high incidence or frequency of cervical cancer have uniformly an early onset of first sexual relationship.

Circumcision

In view of the fact that some degree of circumcision has been practised in the United States for the past 60 years and that among non-Jewish males the rate of circumcised men in the age group of 40 to 70 was shown to be 20%, this factor could be studied among the non-Jewish population groups (Wynder *et al.*, 1954). For the white non-Jewish group 5% of the cases reported exposure only to circumcised males, as compared with 14% of the controls. For Negroes the respective percentages were 0.5% and 9%. Among the

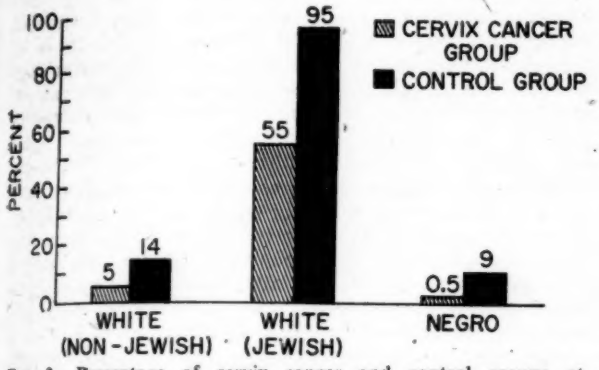

FIG. 3.—Percentage of cervix cancer and control groups at American hospitals exposed only to a circumcised sexual partner.

Jewish controls 95% were exposed only to circumcised sexual partners, in contrast to only 55% among 20 Jewish patients with cancer of the cervix (Fig. 3). Among 20 Jewish patients with cervical cancer, three had been married to uncircumcised non-Jews and six admitted to extensive relationships with uncircumcised partners. The age of circumcision does not seem of importance so long as it occurs before marriage. In India only the Moslems practise circumcision. Moslem boys are circumcised between the ages of 6 and 9. The factor of circumcision was cross-analysed and found to be independently significant.

The most desirable way to study the possible effect of penile hygiene would have been to examine the husbands of the patients studied. Because of the obvious difficulty of such a procedure, we examined males from the general hospital population, dividing them into different economic, racial, and religious groups. The data show that those male groups have the highest degree of poor penile hygiene whose females also have the highest rates of cervical cancer (Table IV). This holds true for the American as well as for the Indian data. It is of interest to note, as judged from the Madras data, that not all circumcisions done on Moslems are complete.

TABLE IV.—*Percentage Distribution of "Smegma Formation" Among American and Indian Males*

	No. of Cases	None	Moderate	Marked
American:				
Non-Jewish white (private)	580	92	7	1
" " (clinic)	125	70	24	6
Jewish	980	99·4	0·6	0
Negro	100	44	48	8
India (Bombay):				
Hindu	130	56	28	16
Christian	50	56	30	14
Parsee	50	94	4	2
Moslem	130	100	0	0
India (Madras):				
Hindu	61	16	66	18
Christian	48	27	63	10
Moslem	31	58	42 (slight)	0

Pregnancy

Several authors have found more pregnancies among patients with cancer of the cervix than among controls, as was indeed also found in this study. For example, in the non-Jewish white group 20% of the cancer group had more than six children, in contrast to 11% among the controls. The respective figures for the Negro cases were 15%

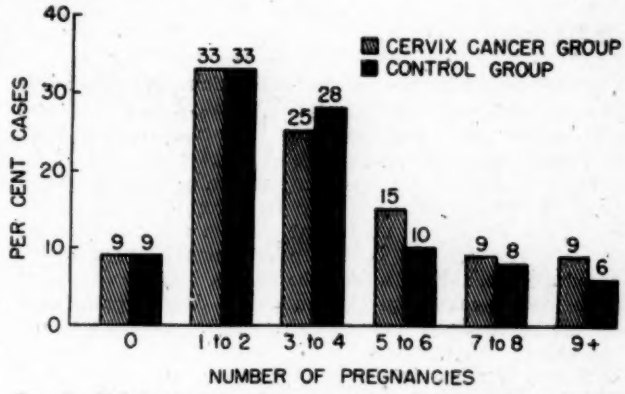

FIG. 4.—Pregnancy rate of cervix cancer and control groups for white non-Jewish women standardized to age of first marriage.

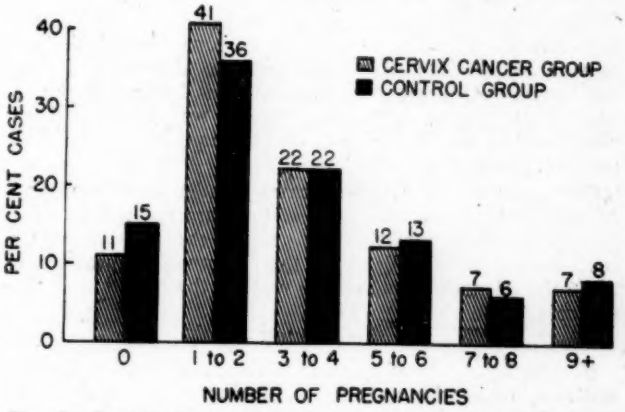

FIG. 5.—Pregnancy rate of cervix cancer and control groups for Negro women standardized to age of first marriage.

and 13%, showing no essential difference. The nulliparous rates for the white non-Jewish group were 9% and 12%, and for the Negroes 11% and 19%. In cross-analysing the data we standardized the number of pregnancies against the age of first marriage, since it was clear from recent studies by the Milbank Foundation that the age of marriage has a significant influence on the number of pregnancies (Kiser and Whelpton, 1944). In Figs. 4 and 5 we present the number of pregnancies standardized to the age of marriage separately for non-Jewish white and Negro cases, and find that there are indeed no significant differences in the rate of pregnancy between cervical cancer and control groups.

Abstinence after Menses

Abstinence from coitus for seven days after the last day of menses, as prescribed by Talmudian law, has often been thought to account for the low rate of cancer of the cervix among Jews (Kennaway, 1948). It was also thought to account for the low rate of cervical cancer among the Parsees. The following points seem to rule out this factor as one of great significance in preventing cervical cancer :

(*a*) Though the law is practised to some extent in the older Jewish age groups, it is generally not practised at all in the younger age groups. Among Jewish controls 30% reported no abstention after menses. Among those who abstained, 40% did so for a full seven days. Of those who abstained over the age of 50, 50% abstained for seven days. The comparative figure for those under 50 was 28%. Very few Jewish women under 40 abstained for the seven-day period. Thus, cervical cancer should begin to increase in frequency in Jewish women if this factor were indeed of great significance.

(*b*) Twenty Jewish cervical cancer cases do not suffice for statistical comparison, but they seem to be in line with the controls. Five of the 20 patients in this group did not abstain after menses.

(*c*) None of the Parsees studied abstained for one week after menses.

Miscellaneous Factors

Other negative factors included douching, hormone therapy, and vaginal discharge. Negative factors found also include onset and regularity of menses, and number of miscarriages and abortions.

There was some difference in the rate of syphilis; however, the data indicated this to be a result of the earlier age of first intercourse among the patients with cancer of the cervix. The role of contraception remains questionable because no reliable data could be obtained on the frequency of the use of contraceptives, though the data suggested that the use of condoms was somewhat greater among the control group. We did question our patients on the frequency of sexual relations in the early part of their sexual lives. We felt, however, that the patient's memory in respect to these data was too hazy to give information which would be useful for statistical analysis.

The presence of cervical laceration could not be studied with any degree of reliability by personal interview, but, in view of the fact that there was no difference in the number of pregnancies, some doubt must be placed on the role of this factor. Chronic cervicitis was as often diagnosed among the Jewish patients as among the non-Jewish patients studied.

The study also included 32 cases of adenocarcinoma and 34 cases of carcinoma *in situ*. These are not sufficient to afford statistical analysis. In general the *in situ* cancer cases tended to be in line with the epidermoid cancer cases, while the adenocarcinoma cases went in the direction of the controls.

Discussion

For statistical association to have also causative significance the association must at least in part explain differences in incidence and frequency patterns. Table V presents

TABLE V

Population Group	Rate of Cervical Cancer	Age of First Coitus	Circumcision State and Penile Hygiene
Hindus (India)	Very high	Very early	Very poor
Negroes (U.S.A.) ..	High	Early	Poor
Christians (India) ..	,,	,,	,,
Moslems (India) ..	Low	Very early	Good
Parsees (India)	,,	,, late	,,
Jews (U.S.A.)	Very low	Late	Very good

evidence suggesting that the factors of age at first coitus and lack of circumcision may account for the differences in rates of cervical cancer. In respect to circumcision, it may well be that good penile hygiene may achieve the same end.

The data suggest that virgins have the least risk of developing cancer of the cervix, whereas those groups practising early relationships and whose males have poor penile hygiene have the highest risks of cervical cancer. These two factors can, in our opinion, account for the observed differences in frequency rates. For example, Negroes tend to have early sexual relations and relatively poor penile hygiene, and have a high rate of cervical cancer. Hindus have an even earlier rate of first intercourse and more extensive bad hygiene, and have the highest rate of cervical cancer. Jewish women have a relatively late age of first marriage, the males practise excellent penile hygiene due to circumcision, and have a low incidence of cervical cancer. Moslems marry quite early yet have only one-third of the rate of cervical cancer as compared with the Hindus. No other differences could be determined between the Hindu and Moslem data except for the circumcision variable. Parsees, with a relatively low incidence of cervical cancer, marry late, and, though they do not practise circumcision, have good penile hygiene. Cancer of the cervix is rare among women without sexual relations, and is quite frequent among prostitutes.

It does not lie within the confines of this communication to speculate upon the mechanisms by which lack of circumcision and early sexual relationships may influence the development of cervical cancer. It may be theorized that under the male foreskin exists a carcinogenic agent. This hypothesis is emphasized by the infrequency of penile cancer among circumcised males and by the fact that horse smegma has been found to be carcinogenic to mouse skin (Plaut and Kohn-Speyer, 1947). Recently, H. R. Pratt-Thomas (personal communication) induced a significant number of cervical cancers in mice with human smegma. It is of interest, too, in this respect that population groups with a high rate of penile cancer also have a high rate of cervical cancer. The fact that the latter is more common than the former may be due to the much greater tissue susceptibility of cervical epithelium to cancer formation.

The earlier onset of intercourse among patients with cancer of the cervix could be explained on the basis of special hormonal patterns or merely as a result of the socio-economic *mores* of a given population group. We believe it to be primarily due to the latter factor, since early coitus seems to be a consequence of socio-economic and conventional standards rather than due to a special hormonal status. It can only be speculated why early intercourse leads to more cervical cancer. It may be due to greater susceptibility of young cervical tissue. It may be because of a more active sexual life in women who marry early. It may be due to a greater variety of sexual partners in women who marry early—a factor which we were not able to study in detail. The fact that cancer of the cervix occurs more frequently, for example, in women who have been married more than once might be on the basis that these women have had two active sex lives, or on the basis that such a woman is more likely to be exposed to a "carcinogenic" male than one who has had only one marriage.

The lack of correlation of pregnancy with the development of cervical cancer is of academic as well as of statistical interest. It demonstrates the importance of properly controlled and analysed environmental studies. It is suggested that if previous investigators had standardized their data to age of first marriage the pregnancy rate of their controls would also have been similar to those of the cervical cancer patients.

Since pregnancy rate, including that of miscarriage and abortion, was demonstrated to be a negative variable, it may be proposed that factors associated with pregnancy, such as cervical laceration and poor prenatal care, may also not be significant in the development of cervical cancer.

Epidermoid Carcinogenesis

The results of this study re-emphasize the data of Pott, other industrial cancer investigators, and recent lung cancer surveys that epidermoid cancer but rarely arises in sites not exposed to extrinsic factors of irritation. The human evidence in this respect is supported by animal data. Spontaneous epidermoid cancers in laboratory animals are quite uncommon. In a large necropsy series (Wells, Slye, and Holmes, 1941) they could find only a few epidermoid lung cancers. Spontaneous skin cancer in mice is very uncommon, though this area is quite susceptible to carcinogens.

From the point of view of practical significance it makes little difference what concept one holds regarding the mechanism which transforms a normal cell into a neoplastic one. It might well be, as Warburg (1954) suggests, that extrinsic factors interfere with the oxidation mechanism of the cells and thus initiate neoplasia. Perhaps at some future date we may uncover the specific mechanism by which certain extrinsic factors may initiate cancer. From the present point of view, however, it is most important to recognize that in the absence of these factors the incidence of some cancers is greatly reduced, and that by their control we are advancing an effective means of cancer prevention.

Epidemiological Considerations

Recent epidemiological surveys on cancer have re-emphasized the significance of properly controlled and conducted clinical studies which, we believe, can add more information about the effect of environmental factors on human cancer than could be obtained from any laboratory experiment. It is a method which requires a close co-operation of qualified statisticians, clinicians, and trained interviewers. Such a team can establish data which can be regarded as experimental as any laboratory work, and thus do not represent "just some statistics." If the data obtained by such an investigation are compatible with the incidence pattern of the cancer, with its geographic distribution, and with its time trends, then, it seems, we are dealing with factors that are not only of statistical but also of causative significance.

Practical Considerations

In environmental cancer work we have to separate data into those of academic and those of practical importance. The factor of age of first intercourse is primarily of the former, whereas those referring to circumcision and penile hygiene are of the latter. The data suggest, though they do not prove, that good penile hygiene may be as effective as circumcision and that this may account for the relatively low frequency of cervical cancer among the high-income groups, a fact which of course may also be influenced by the later onset of marriage as compared with the low-income group (Wynder *et al.*, 1954). The best and most practical measure for obtaining good penile hygiene is universal circumcision. For the past ten years a high degree of circumcision has indeed been practised in the United States. In a recent study based upon reports from 84 hospitals throughout the United States, 85% of all non-Jewish male babies born in the semi-private or private class were circumcised at birth (E. L. Wynder, unpublished data). The circumcision rate was equally high among Protestant and Catholic births. Thus, if it is indeed true that circumcision acts as a preventive measure against cancer of the cervix, a marked lowering should be noted in this type of cancer in the coming generation.

In summary, this study again showed that in the development of epidermoid cancer extrinsic factors are of significance. It was demonstrated that clinical-statistical investigation, provided that it considers all of the environmental factors, can separate those that are independently and those that are only dependently significant. It was shown that factors can thus be determined which can account for marked differences in frequency patterns found among different population groups which previously had been supposed to be on the basis of racial factors. The two most important factors were those of the age of first sexual relations and the lack of circumcision, or the associated poor penile hygiene. Of these two factors, the latter has the greatest practical significance. Even these two factors, of course, represent only a link in the total chain of cancer development, and undoubtedly other factors must be present, though so far they remain unknown to us. However, if by removing a link we can interrupt a chain of development we have succeeded in preventing the chain from undergoing completion. It is along this line that environmental cancer research has its greatest purpose.

Summary and Conclusions

A study of the role of environmental factors in cervical cancer indicates that differences in age of first coitus and circumcision status or lack of good penile hygiene can explain variant incidence data of cervical cancer among different population groups.

There is no statistical evidence that pregnancy rate plays a part in the production of cervical cancer. The data on pregnancy demonstrate the significance of careful statistical analysis in separating the dependent from the independent variables. They clearly emphasize the importance of trained statistical aid in these investigations.

The abstinence period practised by orthodox Jewish women after the end of menses is not believed to be the basic factor accounting for the low incidence of cervical cancer among Jewish women.

The data emphasize that exogenous factors play a major part in the development of epidermoid cancer.

The results underline the importance of international co-operation, which can achieve more conclusive results than can be obtained from any one country alone.

The findings suggest that universal circumcision may be a practical preventive step, significantly reducing the incidence of cervical cancer.

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The downward trend in the total volume of crime in England and Wales, first noted in 1952, continued throughout 1953, according to statistics in the *Report of Her Majesty's Inspectors of Constabulary for the Year ended September 30, 1954.* Offences against property without violence decreased by 8.9%, and offences with violence by 9.5%, including 6,512 fewer crimes of shopbreaking and 1,619 fewer of housebreaking. An encouraging decrease was also shown in the number of boys under 14 and youths under 17 found guilty of indictable offences. Though the figures are still high, 20,774 and 14,549 respectively, compared with those for 1938, it is believed that the post-war wave of juvenile delinquency has at last been checked. The most disquieting feature of the report was the record of continued increase in sexual crimes; sexual offences increased by 9% and offences of violence against the person by 1½% over the previous year. The public's response to the police drive to make them "crime prevention conscious" is one of the main reasons given for the reduction in the total. It is also thought that the building-up of the uniformed branches of the police, the advantage of basic training for young officers, and the still increasing assistance given by the forensic laboratories have proved a deterrent. The preliminary figures for the first nine months of 1954 show that the improvement continues. Of the non-indictable offences, traffic offences decreased by 6%, but gaming and betting offences increased by 7%. There was little change in the number of persons found guilty of drunkenness.

PSYCHICAL PHENOMENA IN TEMPORAL LOBE EPILEPSY AND THE PSYCHOSES*

BY

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The psychical phenomena which form part of the seizure pattern in certain cases of epilepsy may be said to represent a mental disorder in miniature, and for this reason their study may help us to understand the more complex and global mental disturbances found in the psychoses. We claim no originality for this suggestion, for it was made by Hughlings Jackson in 1875. And the Jacksonian epithet, "dreamy state," serves to remind us that Hughlings Jackson was one of the first to stress that psychical phenomena are just as much a manifestation of epileptic discharge as the more spectacular tonic and clonic contractions. Moreover, he was able to correlate such mental concomitants of epilepsy with a structural lesion—since in his famous case of Dr. Z, who suffered from "dreamy states," he and Colman (1898) demonstrated at necropsy a softening in the uncus of the left temporal lobe. These were some of the first stages in a long pathway which has led to present-day investigations into the psychical phenomena in temporal lobe epilepsy—investigations which will always be associated with the name of Dr. Wilder Penfield, of the Montreal Neurological Institute.

Hughlings Jackson and his contemporaries obtained their knowledge from clinical observation and interrogation of the patient during or after the seizure. This must always remain an essential preliminary to any investigation. The proof, however, that such abnormal mental experience is the product of epileptic discharge in the temporal lobe has come from electrical stimulation of the temporal lobe cortex in conscious patients. In particular it has come from the accumulated, carefully controlled, and correlated stimulations carried out in the last 30 years by Penfield and his associates (1941, 1950, 1954) during their operative procedures for the relief of epilepsy. These electrical stimulations are an essential part of the operative technique, their purpose being to delineate the epileptogenic focus, but probably no other routine operative technique arouses such strained suspense in the observer, who knows that at any moment the electrode may elicit from the patient a description of some sudden and compelling mental experience which cuts across his normal stream of consciousness. Thus, for the first time in history, man has been made to see visions and hear voices by means of the stimulating electrode and at the will of the surgeon.

The psychical phenomena which are produced by epileptic discharge in the temporal lobe or by cortical stimulation are many, and include hallucinations of vision, hearing, smell, taste, touch; illusions of distance, size, form, colour, motion, speed of sound and time; disturbances in equilibrium and body image; alteration in thought and affect; disorientation for time, place, and person; disturbances in speech and automatism, the latter with its accompanying memory defects.

From all this bewildering variety we have had perforce to make a selection, and here we propose to illustrate but three, which have a special bearing on the psychoses, in particular on the disturbance in thinking found in schizophrenia.

Material

The cases of temporal lobe epilepsy presented here have been selected from the first 105 cases of a series studied by one of us (S. K.) under the direction of Dr. Wilder Penfield at the Montreal Neurological Institute since September, 1952. Sixty-eight had undergone one or more craniotomies. Nine of the total were tumours, two were cysts, and the remaining 94 were atrophic lesions of the temporal lobes.

The cases of psychoses were studied at the Royal Edinburgh Hospital for Mental and Nervous Disorders, between the years 1946 and 1954, under the direction of Professor Sir David K. Henderson.

The experiences which we describe and illustrate may be stated thus: (1) The experiencing of "thoughts"—such thoughts being either indefinite or formulated. (2) The hearing of "voices" within the mind or body or from a point external to the self. (3) The seeing of persons, objects, or scenes, which, again, may be perceived within the mind or at some point external to the self.

We later present the hypothesis that all these three are but variants of the same phenomenon—that they all represent abnormal derivatives of thought.

1. Evocation of "Thoughts" in Temporal Lobe Epilepsy

We first illustrate these experiences from cases of temporal lobe epilepsy. The first case is one in which "thoughts" occurred as part of the seizure pattern and were also reproduced on cortical stimulation. The "thoughts" so induced were not clearly formulated—they may be called "amorphous" thoughts.

Case 1

A. D. was a young man of 20 who had suffered from both major and minor epileptic seizures since the age of 16. E.E.G. examination revealed an extensive epileptic abnormality in the right temporo-parietal lobes. Before operation he described what he experienced during his seizures as "two thoughts coming together." He explained it thus, "It is something whatever I may be occupied with at present is overlapped or overjoined by another thought. This thought comes along, hits me and goes back, a reminder, but I cannot give a picture of what it reminds me. Something hits me and reminds me of something which hit me before; maybe that is why I think it is two thoughts." This mental experience was followed by a squeamish feeling in his stomach. He remained able to speak and understand throughout the minor seizures.

When, during operation, cortical stimulation was made at a point 6 cm. from the tip of the right temporal pole in the second temporal convolution, at a depth of 1 cm., the patient said, "My thoughts sort of bounced together for a second," but he added that this was not exactly similar to his experience during an attack. Three later stimulations, carried out at variable intervals at a depth of 2 cm. slightly anterior, reproduced, however, a change in thought identical with that which occurred during his attacks. During the first stimulation he said "the same two thoughts which come together"; and when the electrode was withdrawn he explained that one of those thoughts was concerned with what was happening at the present time, and the second thought was of something different, but what it was he could not recall. Stimulated a second time, he said, "This is it," and crossed his index finger over his third in an attempt to illustrate what he meant. When the electrode was withdrawn he was asked whether what he experienced was a memory; he said definitely, "No, it is the thought that crosses." Stimulated a third time, he said, "It comes again," and moved his fingers in

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illustration, saying, "They mixed the thought." This was followed by a feeling in the stomach. This experience of "thoughts" identical to that which formed part of his seizure pattern was reproduced no fewer than three times by cortical stimulation. These evoked "thoughts" forced themselves on consciousness as something separate and distinct from the normal stream of thought of the patient, and were recognized by him as not clearly formulated.

In a second case, both epileptic discharge and cortical stimulation induced the experience of "rhythmic thoughts," which to the patient appeared at the time of their experiencing as fully formulated, although he could not later recall their content.

Case 2

W. S. was an intelligent man of 30 with a left temporal focus. His seizures were ushered in by a sensation in the left chest, and immediately thereafter he was aware that the sounds in his environment—for example, the machinery in his factory—became louder and faster. Human voices, however, did not change. At the same time he experienced "thoughts" coming into his mind—which he described as "rhythmic thoughts—as though I were thinking of something, maybe the rhythm of poetry or music: the rhythm is always the same. It feels familiar to me during the seizure, yet I cannot recall it afterwards." When asked if they were memories, he said, "No, they were like words or combinations of words." On another occasion he added that it was like thinking two things at once. At operation, the pattern of his seizure was best reproduced by stimulation at a point 1 cm. from the tip of the left temporal pole on the second temporal convolution. He was unable to speak during the actual moment of stimulation, but when the electrode was withdrawn he said, "That was something like an attack," and described the sensation in the left chest, and his awareness of "thoughts" entering his mind, the content of which he was unable to recall.

The clinical findings in this case are almost identical with those of a case reported as far back as 1876 by Dr. Coats, of Glasgow, in which the patient's fit was preceded by giddiness and a "peculiar thought." To quote Dr. Coats: the patient "cannot tell what the 'thought' is, yet is confident that it is always the same. He always recognizes it at once when it occurs, and he tries to fix it in his memory, but he invariably forgets when the fit is over."

This induction of thoughts into the mind by cortical stimulation has occurred in other cases, and the stimulation points tend to be grouped around the second and inferior temporal gyri.

It is worthy of emphasis that these patients have difficulty in describing both the content of their induced thoughts and the manner in which they are experienced. This difficulty was well expressed by one intelligent patient, who tried in vain to describe the manner in which thoughts rushed into his mind during his seizures, and finally, in desperation, exclaimed, "It is like asking an artist to paint a picture of what roast beef smells like and he cannot do it." It seems only too probable that what we are asking of them is comparable to the impossible task of describing one sensation in terms of another.

How can we categorize this experience? In what group of abnormal mental phenomena can it be placed? We have of necessity to make use of such concepts as are at present available—although these are less than ideal—and so we would designate these intruding "thoughts" as hallucinations. There is no other word extant—although we hope in future that more precise terms will be formulated—which can cover this experience, whereby a thought, evoked either by epileptic discharge or cortical stimulation, apparently assumes a separate existence alongside the patient's own current of thought. Such separate existence would appear to be proved by the patient's ability to bring his powers of introspection to bear on it, and to describe it, however inadequately, during or after its occurrence.

Definition of Hallucination

According to the Oxford Dictionary, a hallucination is defined as "the apparent perception of an external object when no such object is present," and this placing of the hallucinatory experience outside the self is usually implied in the general usage of the term. It is a finding in psychiatry, however, that when a patient says he "hears" certain words or phrases, that he "sees" certain objects or scenes, what he "sees" and "hears" has for him no external location, but is "heard" and "seen" in the mind. There exists to-day a disinclination to apply the term "hallucination" to these abnormal "*internal*" perceptions, yet the older French writers showed no such hesitation. Baillarger (1890) entitled them "psychical hallucinations" using the contrasting term "psychosensory hallucinations" to designate these abnormal *external* perceptions, which then, as now, were more generally accepted as constituting true hallucinations. Under this title "psychical hallucinations" Baillarger included not only these "alien" ideas which "come to" the psychotic patient in the form of "thoughts," but "voices" which he locates in the head or epigastrium. Séglas (1892) cites, with approval, this category of "psychical hallucinations" first demarcated by Baillarger, emphasizing its clinical authenticity. He himself coined the term "psychomotor hallucinations" to denote the "inner voices" experienced by psychotic patients—believing, in terms of the strict cerebral localization theories popular in his time, that such internal auditory hallucinations resulted from an excitation of the motor centre for speech. Older theories of causation need not concern us here—what is important is that these older writers clearly realized from their detailed clinical examinations that there were varying gradations in the patient's mode of experiencing hallucinations—particularly the so-called auditory hallucinations.

2. "Auditory" Hallucinations in Temporal Lobe Epilepsy

The following case illustrates the hearing of an inner voice *within* the head.

Case 3

W. D. was a youth of 18 who had had seizures for eight years. E.E.G. showed a shifting focus in both temporal lobes. He was bilingual, Afrikaans being his mother's tongue. His seizure pattern was a sensation in his head accompanied by a voice which spoke in Afrikaans, commanding or threatening him. He had a feeling of intense fear and finally lost consciousness. Asked where the voice came from, he said, "It was just in my head." The patient was aware that he could not speak while hearing this voice and felt that his tongue was stiff (a finding common among others who heard voices within the head). He said, "If I heard the voice I used to point to my head so that my parents would know I was going to have an attack." The voice spoke in short sentences which were accusatory or threatening, telling him "You do this" or "You do that," "You did something wrong." "Things," the patient added, "that I did *not* do wrong."

The next case illustrates the hearing of voices within the stomach.

Case 4

M. S. was a little boy of 7, with an eight-months history of epileptic seizures. E.E.G. showed a shifting focus in both temporal lobes. This boy described his experience during the seizure as "I have 'bumps' in my tummy, and I hear 'Do this, do that.'" Asked "Who says 'Do this, do that'?" he replied, "My stomach—I feel something talks in my stomach." On further questioning he said it sounded like a man's voice, but he did not recognize it as the voice of anyone he knew, and that he heard it only in his stomach. Asked whether he ever obeyed this voice, he replied, "I don't do what *he* says, I do what Mummy says." To the question, "Do you think there is a voice in your tummy?" he answered, "Yes—I don't know how *he* gets in there." The commands "Do this, do that," were repeated a few times and were followed by automatism and loss of consciousness. This boy never heard the voice in the intervals between seizures.

This hearing of an inner voice giving unacceptable commands is, of course, typical of schizophrenia, but in both these cases this was a momentary experience, whereas in schizophrenia it tends to be a continuous process. We shall return to this later.

The fifth case illustrates the hearing of an external voice—that is, the experience comes within the commonly accepted definition of auditory hallucinations. (This case has already been reported by Penfield and Jasper (1954).)

Case 5

S. B. was a man whose seizures began at the age of 18, and E.E.G. showed a right temporal focus. The attacks first took the form of vertigo, but a year after their onset the patient, in addition to the vertigo, heard a voice calling his name, "Sylvere, Sylvere," and this was sometimes followed by loss of consciousness. Two years later the pattern again changed, and the aura consisted mainly of a feeling of nausea behind the mid-sternum. At operation, performed six years after the onset of seizures, and four years after the voice calling his name had ceased to be part of his seizure, cortical stimulation reproduced the following:

On stimulation at a point 5 cm. from tip of the right temporal lobe, in the first temporal convolution, the patient said, "Just like someone whispering or something in my left ear—it sounded something like a crowd." Warning without stimulation produced "nothing." When stimulation was made at a point 1 cm. posterior, he said, "Again someone trying to speak to me, a single person." When asked, he added, "Oh, a man's voice—I could not understand what he said." On stimulation at a point 5 cm. from tip of the right temporal lobe on the second temporal convolution, he said, "Someone calling me in my left ear 'Sylvere, Sylvere'—it could have been my brother."

Interesting features of this case are: (1) the hearing of a voice from the side opposite to the stimulation—that is, the phenomenon of lateralization; and (2) the reproduction, by cortical stimulation, of a certain auditory hallucination—to wit, the hearing of a voice calling the patient's name—four years after it had disappeared from the pattern of his seizures.

Penfield and Jasper (1954) have reported the reproduction of auditory hallucinations by cortical stimulation in many cases, and the stimulation points are found to be concentrated around the first temporal gyrus.

These five cases have been selected from many for this one reason—that the five represent a continuous gradation or a spectrum. The epileptic discharge has evoked successively "amorphous" thoughts, formulated or "crystallized" thought, an inner audible voice located in the head, a similar audible voice with an apparent location in the abdomen, and, finally, voices seeming to emanate from the external environment. Cortical stimulation reproduced both the experiencing of thoughts and the hearing of external voices.

Hallucinations in Schizophrenia

We believe that a more complex and less well defined gradation or spectrum can be illustrated in the hallucinations of schizophrenic patients. Here interrogation of the patients presents much more difficulty, for we have to probe beneath a superstructure of delusional misinterpretations and rationalizations to discover the patient's mode of perceiving such hallucinations.

Schizophrenic Thinking

In schizophrenia the patient is continually troubled by ideas which are presented to him independent of his volition. Some appear to him as though emanating from voices in his external environment. These, the commonly accepted auditory hallucinations, represent in our opinion but one gradation of this experience. The term "auditory hallucinations" cannot be made to cover all the modes of perception of this phenomenon, nor does it sufficiently stress its intricate nature, the intimate relationship which exists between it and the patient's own thought. We may illustrate briefly the range of qualitative difference seen in such hallucinations.

In some patients these alien ideas appear as "thoughts" differing only slightly in quality from the silent imperceptible flow of normal thinking. Secondly, they may erupt in consciousness as a formulated word or phrase, with or without some extrinsic quality which the patient describes in terms of known sensations. Patient S. F. said that she experienced "strong thoughts" or "thought forms" which she described as vibrating through her head. She added that the content of these strong thoughts was quite different from what she was thinking at the moment of their appearance—for implicit in this and subsequent modes of experience is the rejection by the patient of these thoughts as his own.

The next gradation occurs when the hallucinatory words and phrases exhibit some kinaesthetic—or verbal—quality which enables the patient to experience them as soundless speech within the mind. I. H., an intelligent nurse of 30, described her mode of perceiving two voices within her mind as follows: "If I compared it to lip-reading, the formation of words without the sound, that is the clearest I can describe it." (There must surely be only a minimal difference in the experiencing of "strong thoughts" and "soundless voices." This is borne out in a famous case, cited by Séglas, of a woman who said that what she heard in her mind was a "voice," and then corrected herself, adding, "No, I am explaining it badly; it is not a voice, it is a suggestion, it is a thought without sound, it is an internal voice which flesh and blood cannot understand—it is a mute voice.")

A further gradation is reached when the patient describes voices, still experienced within the mind, which have superadded to them some subtle quality of sound. W. F. described his experiencing of a voice within his head thus: "I don't actually hear it with the ear—it is not heard outside the head, but it has some sound quality within the head." (It was from this patient's spontaneous description that we borrowed the term "sound quality.") He could not further elaborate it. What seems reasonably certain is that this sound quality does not partake of the tone and timbre of the human voice. A. W. spoke of a "whisper in my head that goes on and on. I don't know where it gets the stamina." This internal voice with a quality of sound may also be experienced in other parts of the body—in the chest or abdomen, as is illustrated by the case of Y. Z., who was suffering from schizophrenia and believed that a certain Dr. T. was in her abdomen. When asked how she knew that, she replied, "I hear him speak and I feel him move." She gave as an illustration that while having a tub bath she heard Dr. T. cry out, "I am drowning." She told him "move up" and he did! This case is almost identical with that of the little boy (Case 4) who heard voices in his stomach as part of his seizure pattern.

The final stage is illustrated in the experiencing of voices which appear to the patient to emanate from his external environment. Some patients unhesitatingly liken these to actual human voices. But others do not display this certainty. They describe a far-away quality—a voice coming from a distance; or, conversely, if near at hand, they use qualifying phrases, such as "like a voice heard through a megaphone." It seems, therefore, that if an auditory component is present it does not always, even in external auditory hallucinations, simulate the tone and timbre of the human voice.

Schizophrenic patients, if carefully interrogated, may admit to experiencing not merely one but two or three of the several gradations above described. There are still further modifications of this phenomenon—for instance, all the patient's thoughts may become verbalized and appear to resound in his external environment—the so-called "echo de la pensée." This necessarily abbreviated account is nevertheless sufficient to indicate the close resemblance which exists between such hallucinations and those found in temporal lobe epilepsy. The "thoughts," the internal and external "voices," which form part of the seizure pattern in the above five cases of temporal lobe epilepsy find their counterparts among the admittedly more numerous and complex modes of abnormal perception illustrated for schizophrenia.

Syntax of "Auditory" Hallucinations

The form of syntax of hallucinations of thought and speech in schizophrenia is difficult, and often impossible, to elicit. It is common but not invariable for patients to describe them as consisting of brief phrases, commencing with pronouns of the second or third person—for example,

"You are," "He or she is," "You did," "Do it." We find striking analogues of these in two of the cases of temporal lobe epilepsy. Case 4 heard a voice in his stomach saying "Do this," "Do that." Case 3 heard a voice in his head saying "You do this," "You do that," "You did something wrong." "Things," the patient added, "that I did not do wrong." This case is of surpassing interest, since not only the syntax, but the content of the patient's hallucinations closely simulates that found in schizophrenia. Here we see evoked by epileptic discharge that specific quality of schizophrenic thinking to which later French writers have applied the term "bipolarity." The content of the hallucinations in schizophrenia tends to consist of ideas that are repugnant or terrifying to the patient, that are the polar opposite of what he himself would wish to think and do. Wherefore he feels constrained to counter them by denial or refusal, and only finally, when their continuous reiteration exhausts him, by acceptance. But acceptance does not terminate this intense mental argument, for new commands and incompatible ideas are evoked, which in their turn engender fresh tension. The patient with temporal lobe epilepsy (Case 3) experienced in episodic form a phenomenon which in schizophrenia may go on every minute, every hour, of waking life, rendering impossible single-minded concentration on all other subjects.

3. Visual Hallucinations

It has been shown that so-called "auditory" hallucinations may be experienced either within the mind or as emanating from the external environment. Visual hallucinations may likewise take the form of internal *or* external perceptions.

(a) In Temporal Lobe Epilepsy

The first gradation of abnormal visual experiencing is illustrated in what patients tend to describe as "flash-backs."

Case A (M. M.) has been reported by Penfield and Jasper (1954). The patient described what she experienced in some of her attacks thus: "Suddenly something flashes through my mind—it is a memory of something past; the experience may last only a few seconds, yet I feel close to that event in my life after it had occurred." She stressed the sudden appearance, brief duration, and extraordinary vividness of this mental image, which was quite different in quality from the ordinary mental pictures which are part of everyone's thinking. Here we have a visual hallucination experienced within the mind.

Case B also illustrates a vivid internal visual experience, with the additional interest of reflecting the patient's immediate interests.

A. R. (Case B) an Englishwoman of 29, was married to a Canadian butcher. She had recently received a photograph of her brother's grave in a military cemetery in Holland. During her seizures she saw, vividly etched on her mind, series of gravestones, rows of tulips, lines of lamb carcasses. She described her manner of experiencing these hallucinations thus: "They were inside my forehead. It was not as though outside on a screen. I did not actually see it in the room; it must have been a mental picture—it came to me without my own powers of direction . . . and it came suddenly." This patient had had seizures since the age of 8, but the induced visual imagery of graves, tulips, and lamb carcasses had only recently appeared as part of her seizure pattern. Her mental preoccupations dictated the content of her visual hallucinations although they played no part in their causation.

Cases C and D experienced visual hallucinations which conform to the accepted definition of hallucinations in that they were apprehended by the patient as though located in his external environment.

Case C is unusual in that it illustrates the transformation of thought into visual hallucinations at the moment of epileptic discharge. There exists a certain analogy between this experience and the "echo de la pensée" of schizophrenic patients, who say they *hear* their own thoughts. This patient *saw* his own thoughts.

D. C. (Case C), aged 16, had an extensive atrophy involving the temporal, parietal, and occipital lobes of the left hemisphere, necessitating their complete resection. Since the age of 8 he had had frequent seizures without loss of consciousness. In the year preceding operation he had three major convulsions. He described what he experienced in these major attacks before losing consciousness. He fell down during the attack and tried to overcome it by mental effort, whereupon he was aware of all his thoughts transforming themselves into vivid external visual images. He was so terrified by this that he kept changing his thoughts, but each thought continued to transform itself into a visual image. For instance, he thought of fire-crackers, and suddenly these were seen in sunset colours of blue and mauve in front of his eyes located "about a block away," seeming to tumble down through the sky but never reaching him. Then he thought of a space ship, and it appeared as a pinkish-blue object, moving towards him, becoming smaller as it did so. He thought of maple trees in the playground, and saw them as though "upside down." (This curious anti-gravity positioning also occurred with a leptazol-induced seizure when he reported seeing the technician as though walking on the ceiling.) Finally, he thought of himself lying on the ground, and immediately saw an external pictorial image of himself, described thus: "The way I felt on the ground was the way I looked in the picture, but people were not around me. I was in different forms; I thought of something, then I saw it. I thought of myself, and then I saw myself the way I was thinking of myself." This occurred with his eyes closed, and the phenomenon disappeared when he opened his eyes, but he said that it was difficult and "unpleasant" to keep his eyes open.

The following case has been reported by Penfield and Jasper (1954).

A. B. (Case D), aged 32, an artist's daughter, had a right temporo-occipital focus. Both simple and complex visual hallucinations occurred as part of her seizure pattern. These included: (*a*) flickering lights seen in the left visual field. (*b*) Representations of famous paintings—Rembrandt's "Night Watch" and "Self Portrait." She also saw, as though in a picture, "Christ coming down from the sky." All these were two-dimensional and were seen in the left visual field, as if superimposed on the existing external environment. (*c*) A kitchen in the country, and she felt—although she did not see—herself there, with two boys running towards her. The kitchen and the boys appeared in three-dimensional form. Unlike *a* and *b*, this image was seen in both visual fields, and during its appearance the patient was blind to all else in her external environment.

(b) In Schizophrenia

Only brief reference can be made to visual hallucinations in schizophrenia. Generally accepted as being a less constant symptom than "auditory" hallucinations, they can on occasion assume predominance. All the visual phenomena described in temporal lobe epilepsy have been found in schizophrenia. There may occur in the latter disease many more varied and complex visual hallucinations. Bizarre hallucinations of parts of the human body are frequent. The patient may have a vision of the self—that is, autoscopic hallucination—but a somewhat similar phenomenon has been elicited in temporal lobe epilepsy (Case C). In temporal lobe epilepsy such hallucinations are an episodic occurrence, whereas in schizophrenia they are a constantly recurring experience; but in both they are of brief duration—"they come and go in a flash"—and in both they may be "seen" in the mind or in the external environment.

Basis and Unitary Nature of the Hallucinations Described

These psychical phenomena—or hallucinations—may be illustrated in the form of a spectrum at one end of which the hallucinatory experience is apprehended as "thoughts," and at the other end as visual or auditory images with an apparent location in the external environment. Intermediate are these visual and auditory abnormal perceptions—or hallucinations—which the subject experiences within his mind. The similarity which exists between these hallucinations in temporal lobe epilepsy and schizophrenia makes it difficult to avoid the inference that the latter disease is also based on some neurophysiological change, the nature of which is yet unknown.

We also submit that all these abnormal experiences are based on a single phenomenon, showing gradations in its mode of perception by the subject; or, in other words, that they all represent but different modes of perceiving abnormal derivations of thought. How, then, can we explain the various gradations? We think it is possible to do so by considering, in its simplest terms, the process of normal thinking.

Some part—the greater part—of normal *thinking* consists in the intangible, imperceptible linkage of elements which cannot be described in terms of known sensations. But there are superadded qualities in thinking which can be termed kinaesthetic and visual. Part of our thinking consists in the evocation of words and visual images. This is illustrated in the division of human beings into "verbalizers" and "visualizers." It seems permissible, therefore, to assume that when some physical stimulus acts on certain areas of the brain to produce an abnormal thought—a hallucination of thought—such hallucination may present (*a*) as a thought—which forces itself on the attention of the subject, cannot be banished or superseded at will as in the manner of normal thought, but is nevertheless incapable of description in other terms than that of "thought"; or (*b*) as a visual or verbal image—of varying degrees of intensity, which the subject describes in terms of vision or hearing.

Summary

A comparison is made between certain hallucinatory phenomena or, more properly, the patient's mode of perceiving certain hallucinatory phenomena—in temporal lobe epilepsy and schizophrenia. The current popular definition of a hallucination, which implies the location of the abnormal perception external to the self, is criticized, and it is submitted that abnormal internal perceptions can also be included under the designation of hallucination. This designation, however, lacks precision, and it is hoped that in future more precise terms will be formulated to cover the many varieties of abnormal perception here illustrated.

Five cases of temporal lobe epilepsy are described in which epileptic discharge evoked respectively (*a*) ill-defined or "amorphous" thoughts, (*b*) formulated or "crystallized" thoughts, (*c*) a voice located in the head, (*d*) a voice located in the abdomen, and (*e*) a voice heard in the external environment. Cortical stimulation reproduced *a*, *b*, and *e*. Similar gradations in this type of hallucinatory experience, elicited from interrogation of patients suffering from schizophrenia, are briefly tabulated.

Four cases of visual hallucinations in temporal lobe epilepsy are described. In two of these the visual experience was apprehended within the mind of the patient, and in the third as superimposed on the external environment. (This last was reproduced by cortical stimulation.) In a fourth case the patient experienced the transformation of all his thoughts into vivid external images—"What he thought, he saw." This bears a certain analogy to the phenomenon known as "echo de la pensée" found in schizophrenia.

It is submitted that these various gradations from "thoughts" to external auditory and visual hallucinations represent but different modes of perceiving abnormal derivatives of thought or hallucinations of thought. Since some part of normal thinking consists in the evocation of visual images and words, it is argued that a hallucination of thought may present either as a "thought" or as a visual or verbal image of varying degrees of intensity.

The finding that epileptic discharge and cortical stimulation can evoke gradations in hallucinatory experience similar to those found in schizophrenia suggests that the latter disease may also have a neuro-physiological basis.

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CHRONIC PAIN IN THE RIGHT ILIAC FOSSA*

BY

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Chronic pain in the right iliac fossa constitutes a common problem in all branches of medical practice. The correct management of the disorder depends upon careful clinical evaluation, and mistakes are easy to make. One common mistake is the tendency among many people to rush into the much abused diagnosis of a "chronic appendix" or, as the only alternative, to treat the patient as a "neurotic." Either of these assumptions may lead to disastrous consequences, and to avoid such obvious pitfalls it is my practice to approach the problem of diagnosis by seeking the answers to three questions: (1) Is there an organic cause for the pain *apart from* the appendix? If not, (2) Is the appendix genuinely at fault? Or, (3) Is the pain of functional origin? This order of questioning has been chosen deliberately, because it often happens that the appendix is removed when some other cause for the pain is present, and because it too often happens that the appendix is removed without reasonable evidence that it is diseased. Functional affections, however, should always be considered last, because there can be no greater error than to stigmatize a patient "neurotic" when in fact organic disease is present.

1. Causes of Pain Apart from the Appendix

Let us first consider those organic causes of chronic pain in the right iliac fossa which are unconnected with appendicular disease. So that nothing of importance shall be omitted, it will be convenient to classify them on an anatomical basis.

(*a*) *The Caecum.*—There is no doubt that chronic pain in the right iliac fossa can arise in the caecum. It may be due to *gaseous distension*, when the area is tympanitic, gurgling is present on palpation, and excessive borborygmi are heard on auscultation of the abdomen. In older patients it must always be borne in mind that caecal distension may signify chronic intestinal obstruction due to a carcinoma of the pelvic colon, and every effort must be made to exclude this serious disease. *Loading* of the caecum with soft faeces, in association with constipation, may also cause chronic pain in the right iliac fossa; in these cases a characteristic doughy feeling is detected on palpation. Pain may also arise from caecal *spasm* accompanying general

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colospasm; tenderness is present over the caecum and often over a rigid pelvic colon in the left iliac fossa. In such cases propantheline (" pro-banthine "), a recently developed ganglion-blocking agent, is of great diagnostic and therapeutic value. *Malignant disease* of the caecum seldom causes pain as its first symptom.

(*b*) *The Terminal Ileum.*—Chronic pain in the right iliac fossa is rarely due to disease of the terminal ileum. *Crohn's disease* (regional ileitis) may give rise to an attack of acute or subacute pain closely resembling appendicitis, but in its chronic form it produces the symptoms of chronic small-intestinal obstruction with recurrent attacks of colicky pain in the right iliac fossa. Young adults are usually affected, and loss of weight is common. The thickened terminal ileum is usually palpable as a tumour in the iliac fossa. A similar history of recurrent bouts of colic occurs with localized *tuberculous enteritis*, but here no tumour is palpable. Both these diseases are rare, but they should be considered in the differential diagnosis of difficult cases.

(*c*) *Mesenteric Glands.*—Enlargement of the ileo-caecal glands is a common cause of pain in the right iliac fossa in children. Pain arising in these glands is due to inflammatory disease and may be tuberculous or non-specific. In *non-specific mesenteric adenitis* pain may be felt in the iliac fossa or in the umbilical region, and may be colicky in nature; there is no shifting of the pain as in appendicitis, and vomiting is rare. Tenderness and muscular guarding are present, but there is no true muscular rigidity. The glandular infection often follows a sore throat and there is usually evidence of chronically infected tonsils. *Tuberculous adenitis* is more difficult to diagnose with accuracy, although a positive Mantoux reaction in young children is suggestive. Radiography is of little use in diagnosis because calcified (healed) glands produce no symptoms. A pale fatty stool due to blockage of lymphatic vessels (tabes mesenterica) is evidence of gross tuberculous disease.

(*d*) *The Urinary Tract.*—Chronic *pyelitis, stone in the ureter, and hydronephrosis* may all cause pain in the right iliac fossa. Frequency of micturition almost invariably accompanies *chronic pyelitis*, and pus cells and organisms are present in the urine. Pain arising from a *ureteric calculus* usually radiates from the loin to the groin, but when a stone becomes impacted in the ureter the pain may be localized to the iliac fossa. In such cases a previous history of ureteric colic is of the utmost importance and the urine should be searched for red blood cells. Chronic or intermittent *hydronephrosis* may cause great difficulty in diagnosis when the pain is not felt in the loin, because associated urinary symptoms are usually absent. Careful bimanual palpation of the loin must be carried out, and in all doubtful cases the urinary tract must be investigated completely.

(*e*) *Female Pelvic Organs.*—Gynaecological conditions are a fairly common cause of pain in the iliac fossa, but the differential diagnosis of these conditions must rest with the specialist. The classical ovarian pain of " Mittelschmerz," spasmodic and congestive dysmenorrhoea, uterine fibroids, pyosalpinx, small ovarian cysts, and prolapse of the ovary come readily to mind. As a generalization it can be said that gynaecological causes of pain in the right iliac fossa should be considered only if the attacks of pain bear a definite relationship to the menstrual cycle, if there is some associated disorder of menstruation, or if a swelling in the pelvis is detected on rectal or vaginal examination. Pain in the iliac fossa associated with a vaginal discharge does not justify a diagnosis of salpingitis.

(*f*) *The Spine.*—Chronic pain in the iliac fossa may also arise from affections of the spine. A *psoas (tuberculous) abscess* will cause pain in the lower quadrant of the abdomen and will be associated with a palpable swelling, but backache is usually the first symptom and the lumbar spine will be rigid when movements are tested. *Congenital or acquired deformities* and *arthritis of the spine* may give rise to pain radiating to the iliac fossa, but a careful analysis of the pain will reveal its radiating character and direct attention to an examination of the spine.

A formidable number of causes of chronic pain in the right iliac fossa have now been discussed, but they must all be given careful consideration in the diagnosis of this symptom. Investigation must always include a detailed and accurate history, careful inspection and palpation of the abdomen, the performance of rectal and vaginal examinations, examination of the spine, and testing of the urine, both chemically and in the laboratory. If all these investigations are negative the next question must be posed—is the appendix genuinely at fault?

2. The " Chronic Appendix "

The term " chronic appendicitis " is misleading and is often used without any serious consideration of its meaning. Some people believe that chronic appendicitis is a clinical entity of common occurrence, others that there is no such disease. A well-known teacher has said that an honest surgeon up to the age of 35 would refuse to believe in the existence of chronic appendicitis; that between the ages of 35 and 40 he would wonder if it occurred but refuse to accept a fee for removing the appendix; and that over the age of 40 he would be convinced that it was indeed a clinical entity.

To try to understand the meaning of the terms " chronic appendix " and " chronic appendicitis " let us consider the common clinical syndromes which occur in appendicular disease. Apart from acute appendicitis, which we are not considering in this discussion, two definite clinical syndromes can be recognized—recurrent subacute appendicitis and recurrent appendicular colic. By *recurrent subacute appendicitis* we mean recurring mild inflammation. In the earlier of these attacks the pain begins in the epigastric or umbilical regions and settles down in the right iliac fossa; in later attacks this shifting character is often absent and the pain is felt in the iliac fossa from the beginning. Fever is slight or absent, but the tongue may be furred and the appetite lost; vomiting is uncommon. Examination of the abdomen during an attack will show tenderness and guarding in the iliac fossa, but no rigidity. Such mild attacks usually last for 12 to 36 hours and then subside, leaving the patient free of symptoms for many months or even years. With *recurrent appendicular colic* the pain is felt around the umbilicus, but tenderness and guarding are present in the right iliac fossa. The pain is spasmodic in character, often more severe than the inflammatory pain of mild appendicitis, and vomiting is common. There is no fever and the tongue is clean. The bouts of colic may last for a few days at a time, and the intervals of freedom between attacks are usually shorter than those between attacks of inflammatory disease.

In the intervals between recurrent bouts of appendicular inflammation or colic the patient may show no abnormal physical signs whatever. The diagnosis depends upon an accurate history and upon observations made by the practitioner during one or more of the attacks; the importance of such observations cannot be overemphasized, and without them the consultant may have great difficulty in deciding the nature of the attacks.

Recurrent subacute appendicitis and recurrent appendicular colic may be considered to represent two types of " chronic appendix," inasmuch as the appendix is repeatedly giving rise to trouble or " grumbling"; but cannot truly be called " chronic appendicitis " because this term implies persistent chronic inflammation of the appendix. It sometimes happens, however, that after repeated bouts of mild inflammation or colic there may be persistent pain and tenderness in the iliac fossa between the main attacks. To this state of affairs the term " chronic appendicitis " might reasonably be applied.

Lastly, we must consider those patients who complain of chronic pain in the right iliac fossa without any definite preceding " attacks " to suggest recurrent inflammation or colic. The pain of which they complain may show occasional remissions, but often it persists for weeks on end,

though sometimes occurring for only short periods during a day. Such patients may show localized tenderness in the region of the appendix but no other abnormal physical signs. Can they be said to be suffering from "chronic appendicitis"? These cases are certainly the most difficult to assess, but increasing experience soon tends to dispel any scepticism about the existence of this type of appendicular disease. We have all had our share of surprises in this field. Patients about whom we were extremely doubtful before operation have shown unexpected pathological changes in the appendix; others who have had an apparently normal appendix removed have been magically cured of their symptoms. In all such patients the history is usually vague and inconclusive. Diagnosis depends upon the single physical sign of persistent localized tenderness and upon our assessment of the type of patient with whom we are dealing; here again the general practitioner can be of enormous help to the consultant with his knowledge of the domestic and personal background of his patient. Clinical impressions of this type assume great importance when we consider that accessory aids to diagnosis are often of little value. Radiographic examination of the appendix is uncertain and its results are often equivocal.

From this discussion the position with regard to the various types of "chronic appendix" may be summarized as follows: (*a*) With a history suggesting *recurrent subacute appendicitis or recurrent appendicular colic* we are on safe ground in advising removal of the appendix. (*b*) A similar history followed by the development of persistent pain and tenderness in the right iliac fossa may reasonably be called *chronic appendicitis*, and here again appendicectomy can be safely advised. (*c*) *Chronic appendicitis* without a previous history of recurrent "attacks" of pain is a more difficult problem. Children should always be given the benefit of any doubt, but in adults the decision to advise removal of the appendix will rest largely upon the general practitioner's knowledge of his patient's character and his interpretation of the nature of the symptoms.

3. Functional Pain

Last of all we come to those patients with no evidence of organic disease apart from the appendix and in whom we are not satisfied that the appendix itself is genuinely responsible for their symptoms. Few patients with pain in the right iliac fossa are true malingerers, and if we are correct in assuming that there is no organic cause for their pain we are dealing with examples of the *anxiety state*.

These patients have genuine symptoms and need help, but great patience and tact are required if that help is to be given. It is surprising how often a sympathetic attitude will reveal a psychological basis for the symptoms, and sometimes the mere unburdening of his troubles will help the patient enormously. Some people are quickly assured if they are satisfied that we have made a thorough and complete examination and can convince them that there is no evidence of serious disease. Others are more difficult to manage and do not readily accept the idea that their pain is nervous in origin in spite of a completely negative examination and a series of negative investigations. The psychiatrist cannot help if the patient is uncooperative, and if our common-sense approach to the mental problem does not produce conviction we are likely to have a dissatisfied patient. But at all costs we must avoid advising appendicectomy in someone we know to be a true neurotic.

All too often such patients will continue to seek further opinions until they find someone who will remove the appendix, but we must not be responsible for such action if we consider it ill advised. It is better to lose a disgruntled patient than to have him return with the same pain after an operation to which we have agreed against our own judgment. It is also better to lose such a patient than to be responsible for that dreadful sequence of events which culminates in subsequent operations for adhesions or other mythical maladies and leads to the creation of a confirmed hypochondriac.

GENERALIZED HYPERTROPHIC OSTEOARTHROPATHY IN ASSOCIATION WITH BRONCHIAL CARCINOMA

A REVIEW, BASED ON 24 CASES

BY

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During the past seven years we have encountered in the West of Scotland no fewer than 24 examples of generalized hypertrophic osteoarthropathy in association with bronchial carcinoma. As it would appear to be the largest reported collection of patients suffering from this fascinating syndrome, and because modern surgery may handsomely reward early clinical recognition, it seems to be an opportune time to review the known facts and some theories of pathogenesis.

While the literature on the subject of generalized osteoarthropathy continues to grow, there has been little increase in our knowledge of the cause and real nature of the pathological changes of this condition since the first known description by von Bamberger in 1889. Marie (1890) named the syndrome "hypertrophic pulmonary osteoarthropathy" and defined it as a "symmetrical osteitis of the four limbs chiefly localized to the phalanges and terminal epiphyses of the long bones of the forearm and leg, sometimes extending to the roots of the limb and flat bones and accompanied by a dorsal kyphosis and some affection of the joints." This description requires little alteration to-day.

Although Hippocrates (1923), as early as the fifth century B.C., had described clubbing of the finger-nails, it was not until late in the nineteenth century that von Bamberger and Marie drew attention to the changes in the extremities associated with certain diseases. The confusion existing prior to Marie's description is illustrated by a case described by Saundby (1889) as one of acromegaly: a man aged 37 with thickening of the hands and joints died after five months, and necropsy showed "a sarcoma of the left lung with caseating pneumonia, a discovery which could only be coincidental." His illustrations put beyond doubt that he had unwittingly dealt with a case of osteoarthropathy.

Numerous reports have appeared dealing with the association of arthropathy with a variety of internal diseases. These diseases have most frequently affected the respiratory tract. Chronic lung abscess, putrid bronchiectasis, and empyema, all now fortunately rare, predominated. Brooks (1913) and Locke (1915) pointed out that at least a proportion of cases of osteoarthropathy had a malignant chest lesion. We have found it in a patient with metastatic lung tumours, and it has been reported in association with such intrathoracic lesions as arteriovenous aneurysm of the lung (Adams *et al.*, 1944), fibroma of the visceral pleura (Price-Thomas and Drew, 1953), and benign tumours of the lung and chest wall (Van Hazel, 1940).

It is interesting to note that osteoarthropathy has been described in a dog with a bronchial carcinoma (Wissing and Weisz, 1943) and in rats (Sutro and Pomerantz, 1939), a horse (Liénaux, 1909), and even a lion (Ball and Lombard, 1926).

It has been witnessed in many apparently unrelated diseases such as carcinoma of the nasopharynx, myeloid leukaemia, colitis, and steatorrhoea. Although a few cases of idiopathic osteoarthropathy have been recorded (Freund, 1938; Camp and Scanlan, 1948) one should hesitate in making such a diagnosis until a primary disease has been excluded. The fickleness of the syndrome is well illustrated by Locke's account of a patient who had osteoarthropathy for five years before a lung tumour became obvious. Such an experience was repeated in one of our series (Case 14); it was nine months before there was radiological evidence of a lung tumour.

Craig (1937), Rottjer *et al.* (1946), Temple and Jaspin (1948), Pattison *et al.* (1951), and Ellman (1953) have all reported a small series of cases of bronchial carcinoma having joint symptoms as the presenting feature. The syndrome is seldom encountered by general physicians, and a possible reason is that the rapidly growing or oat-celled growth, common in the medical wards, does not produce osteoarthropathy. Conversely, in chest-unit patients the more chronic epidermoid variety predominates, and so it is difficult to estimate the frequency of the syndrome in all cases of lung cancer. Jack (1952) found three fully developed cases in 668 patients with bronchial carcinoma. Wierman *et al.* (1954) report an incidence of 5% in 481 resections for malignant lung

Summary of 24 *Patients having Joint Symptoms Related to Lung Cancer and showing Clinical and Radiological Evidence of Hypertrophic Pulmonary Osteoarthropathy*

Case No.	Age	Tumour Site	Histological Type of Tumour	Initial Symptoms and Signs	Duration of Joint Symptoms Before Correct Diagnosis Made	Treatment	Result (To November, 1954)
1	45	R.U.L.	Adenocarcinoma	Radiological shadow for 18 months	5 months	Pneumonectomy, 1947	Operation death
2	51	L.L.L.	Epidermoid	"Rheumatic fever"	7 ,,	Pneumonectomy, 1948	,, ,,
3	47	R.U.L.	—	Stiffness and swelling of ankles and knees	5 ,,	Radiotherapy	Gold therapy produced a remission of joint symptoms. Died with metastases 4 months after start of treatment
4	64	R.L.L.	—	Stiffness, swelling, and pain in ankles and knees	5 ,,	,,	No relief of joint symptoms. Died with metastases 3 months after start of treatment
5	47	R.L.L.	Epidermoid	Stiffness and pain both legs. Also haemoptysis	4 ,,	Pneumonectomy, 1949	Complete and immediate relief of joint symptoms. Died 3 months after operation with cerebral metastases
6	56	L.U.L.	Adenocarcinoma	Haemoptysis	3 ,,	Pneumonectomy, 1950	Complete relief of joint symptoms. Died 7 months after operation with cerebral metastases
7	53	R.L.L.	,,	Pain and stiffness of knees	3 ,,	Lobectomy, 1949	Immediate relief of joint symptoms which, however, recurred with the appearance of osseous metastases. Died 8 months after operation
8	52	R.L.L.	Epidermoid	Pain and swelling of wrists, feet, and ankles	10 ,,	Pneumonectomy, 1949	Immediate and permanent relief of joint symptoms. Died 6 months after operation with local recurrence of tumour
9	59	R.L.L.	Adenocarcinoma	Haemoptysis	4 weeks	Pneumonectomy, May, 1951	Immediate relief of joint symptoms. Some residual stiffness of left shoulder and slight deformity of fingers. Has remained well since operation
10	59	R.L.L.	Epidermoid	Pains in legs and swelling of ankles and knees	5 months	Pneumonectomy, Sept., 1947	Has remained symptom-free since operation
11	38	L.U.L.	,,	Stiffness of ankles and knees	6 ,,	Pneumonectomy, Jan., 1952	Immediate disappearance of joint symptoms. Died October, 1952, with local tumour recurrence
12	52	R.L.L.	,,	Stiffness of arms and legs	2 years	Symptomatic	Died 2 months after first seen and diagnosed
13	41	R.U.L.	,,	Stiffness, pain, and weakness of knees and ankles	5 months	Radiotherapy	Partial remission of joint symptoms and of chest pain. Died with cerebral metastases 12 months after diagnosis made
14	46	R.L.L.	,,	Stiffness and swelling of knees	10 ,,	Pneumonectomy, April, 1952	Relief of stiffness and pain. "Weak joints" remained after operation. Ultimate complete rehabilitation. Died December, 1953, with cerebral metastases
15	54	L.U.L.	—	Left shoulder pain	3 weeks	Radiotherapy	Partial relief of joint symptoms with corticotrophin. Complete and permanent relief after radiotherapy. Died with local tumour extension 9 months after diagnosis made
16	50	R.U.L.	Epidermoid	Lassitude and weight loss	4 months	Symptomatic	Died 2 months after diagnosis made
17	48	R.L.L.	,,	Haemoptysis	4 ,,	Lobectomy, Sept., 1952	Immediate relief of joint symptoms. Died with generalized metastases December, 1953. No recurrence of rheumatism
18	56	R.U.L.	,,	Pain and stiffness left shoulder and cough	12 ,,	Thoracotomy, Oct., 1952	Partial spontaneous remission of joint symptoms before operation, and continued improvement after thoracotomy. Died April, 1953, with metastases
19	52	R.L.L.	,,	Cough and chest pain	5 ,,	Thoracotomy, Feb., 1953	Spontaneous remission of joint symptoms preceded operation. No recurrence before death from metastases January, 1954
20	49	L.L.L.	,,	Stiffness and pain in hips, knees, and wrists	6 weeks	Lobectomy, May, 1953	Immediate complete relief of joint symptoms. Has remained well to date
21	55	L.U.L.	,,	Swelling and stiff- of ankles	6 months	Pneumonectomy, July, 1953	Relief of polyarthritis symptoms. Myocardial infarction with congestive failure during convalescence. Died with cerebral metastases March, 1954
22	57	L.L.L.	,,	"Arthritis" left knee	16 ,,	Symptomatic	Admitted to hospital in terminal stages of illness with massive left pleural effusion. Died after 2 months' observation
23	62	R.U.L.	,,	Generalized joint stiffness	3 ,,	Pneumonectomy, July, 1953	Immediate disappearance of joint symptoms. Died with metastases April, 1954
24	57	L.L.L.	,,	Swelling of knees	3 ,,	Lobectomy, Nov., 1953	Had usual relief of "rheumatism" and has remained well to date

lesions, but these included patients with so-called "local osteoarthropathy" or simple clubbing. It is our impression that the frequency of the generalized form is in the region of 1–2%.

Clinical Manifestations of Osteoarthropathy

From the Table it will be seen that 16 patients had joint disability as the first evidence of disease. Case 12, for instance, had stiffness for a year before the first symptoms directly related to the lung tumour appeared. All 24 patients had experienced such "rheumatic" symptoms for an interval, varying from 3 weeks to 16 months, before the presence of a tumour was suspected. Stiffness and swelling of the large and small joints of the limbs were the usual complaints; pain may be severe or be present only with joint movement, or it may be absent. Four of the patients were completely crippled and confined to bed. Sensations of warmth or burning and increased moisture of the hands and feet were sometimes volunteered.

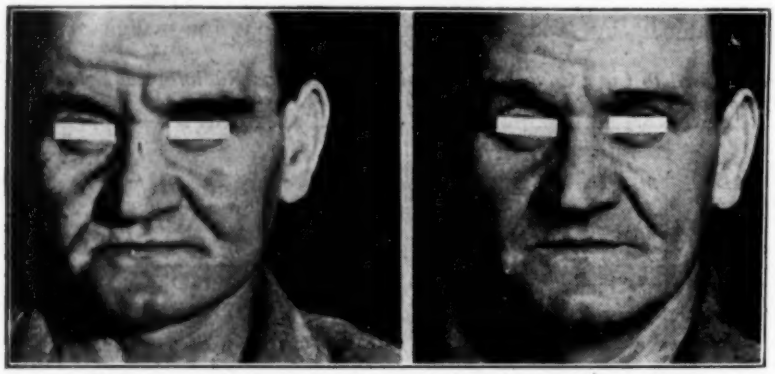

FIG. 1.—Clinical photographs of Case 14, illustrating (left) the furrowed and coarse features sometimes seen with osteoarthropathy, and (right) the same patient four months after right pneumonectomy.

Skin around the affected joints may show thickening and brawny oedema. A similar change is sometimes found on the face, producing rather a characteristic coarse, furrowed appearance (Fig. 1), already observed by Fried (1943).

The hands may have a rheumatoid appearance or be spade-like as in acromegaly (Fig. 2). Hands and feet are warm and moist, and pulsation may be felt in the palms and fingers and heard with a stethoscope on the brachial or femoral artery. Capillary pulsation, however, is not a feature.

Finger-clubbing is almost invariably associated with osteoarthropathy, and occasionally is the most obvious feature clinically; on the other hand, it may be very mild in degree. Conversely, it is known that advanced clubbing may occur in certain types of chronic lung and congenital heart disease without evidence of periosteal reaction or joint disability. Clubbing therefore should not be considered synonymous with osteoarthropathy, nor even necessarily the earliest stage of it (Hansen, 1954).

There may be a low-grade pyrexia, and a raised erythrocyte sedimentation rate is invariable, but these, and especially the latter, are common findings with bronchial carcinoma. Swelling of the nipples occurred in two of our patients. Stephens (1928) reported an incidence of 7% with gynaecomastia in a series of 156 cases of bronchial carcinoma.

Response to Treatment

Remission of joint symptoms may occur spontaneously (Cases 18 and 19), and some relief may be obtained from nitrogen mustard (Case 8), gold therapy (Case 3), and corticotrophin (Cases 14 and 15). Some patients treated by deep *x*-ray therapy had partial or complete relief of "rheumatism," but the objective signs of osteoarthropathy were little altered.

The most dramatic, immediate, and complete relief of joint symptoms is produced by operative removal of the lung tumour. In all 13 patients who survived tumour resection, joint mobility was increased within hours of the operation, and the patients who had been bedridden with "arthritis" for weeks or months were walking normally within a few days. It is no exaggeration to state that these patients were dumbfounded at the relief, and more than once we found them the morning after operation studying the increased mobility of their fingers and arms in utter amazement. Just as rapidly, they remarked that their hands and feet felt more cool, and objectively we could no longer find evidence of increased peripheral blood flow. Joint swelling subsided in a matter of days; in a few weeks, thickening of the skin of the face and around the joints had disappeared and clubbing subsided (Figs. 1 and 2). After a few months, radiological examination showed absorption of subperiosteal new bone (Fig. 3) and disappearance of osteoporosis in the wrist bones.

FIG. 2.—Case 14. Patient's right hand (A) before operation, showing the spade-like deformity, with clubbing and thickening around the wrist- and finger-joints. Same hand (B) seven months after pneumonectomy.

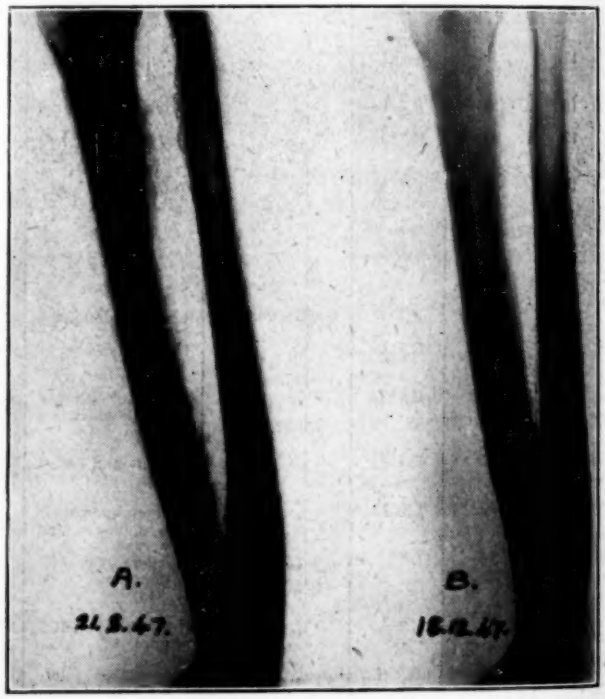

FIG. 3.—Case 10. Right radius and ulna before operation (A): note the marked subperiosteal proliferation. Film (B) three months after pneumonectomy shows considerable absorption of this new bone.

One patient (Case 7), who had obtained the usual relief from lung resection, had a relapse of "arthritis" associated with the appearance of metastases: however, this was an exception, as other patients who died from local tumour recurrence or from metastases had no such relapse before death.

Death was invariably related to tumour spread and there was little evidence that these tumours behaved differently from the more usual case of slowly growing epidermoid carcinoma. Indeed, operative results have been disappointing, only 4 out of 15 patients treated by resection being alive.

Biochemical Findings

In common with previous observers, we have found essentially normal results in most estimations carried out for the study of metabolic bone disease. An exception was the serum phosphorus level, which was found elevated in four severe cases studied. Excretion of F.S.H. (follicle-stimulating hormone) was normal, but this test brought to light a finding which may be of practical importance: in two cases the patient's urine, extracted for the hormone, appeared to contain an unidentified substance which was lethal to laboratory mice.

Arteriovenous oxygen difference was found to be very low in two patients, and in one other the figure rose abruptly after operation. This finding and increased peripheral blood flow, along with absent capillary pulsation, suggest the presence of arteriovenous shunts by-passing the capillary bed.

Skeletal and Articular Changes

The bone changes of osteoarthropathy have been adequately described by past observers (Compere *et al.*, 1935; Gall *et al.*, 1951). There is a proliferative periostitis, characterized by lymphocytic and plasma-cell infiltration, subperiosteal new bone formation, and the production of a pseudo-cortex, 1 to 5 mm. thick, which ultimately fuses with and expands the cortex. It particularly affects the lower ends of the forearm and leg bones, metacarpals, and metatarsals. In extreme cases, clavicles, ribs, pelvic bones, scapulae, and malar bones may be involved. Radiologically (Fig. 3) the picture is quite characteristic, and is perhaps most like a yaws periostitis, showing an irregular but symmetrical osteoid sheathing of the long bones. Joints in involved extremities show extra-articular thickening, but may be the seat of mild to moderately severe chronic synovitis, associated with non-specific degenerative changes in the articular cartilages. In advanced cases, deformities and even subluxations may occur. Changes in the carpus and tarsus are of an osteoporotic character.

Lung Tumour Features

Most of our patients had bulky, circumscribed peripheral neoplasms. Of these studied histologically, 17 were of epidermoid type and four were adenocarcinoma. Central necrosis was a feature in all operation and necropsy specimens. The tumours were present in the right upper lobe (6), right lower lobe (10), left upper lobe (4), and left lower lobe (4). As this type of neoplasm rarely produces atelectasis or invasion of neighbouring structures in the earlier stages, clinical silence is the rule, and yet the patient may be a helpless cripple from his associated arthropathy.

Illustrative Case Histories

Case 7.—An electrical engineer aged 53 was admitted to hospital in January, 1949, complaining of pain in his left chest for a month, pain and stiffness of his knees and swelling of the finger ends for three months, and swelling of the ankles and feet for one month. *X*-ray examination showed a circumscribed dense homogeneous shadow in the posterior basal segment of the right lower lobe and the changes of osteoarthropathy in the long bones. There was marked clubbing of the fingers and toes and tender extra-articular thickening around both knee-joints. Bronchoscopy showed tumour tissue in the orifice of the right posterior basic segment orifice (histologically adenocarcinoma). He had a right lower lobectomy on March 1, 1949, and the following day his knees and ankles were much less stiff. Convalescence was uneventful and the joint symptoms disappeared completely. Six months later, however, he developed pain in his left elbow, and *x*-ray examination showed a metastasis in the lower end of the humerus. From then until his death in November he had a marked exacerbation of the joint symptoms. Two weeks before death he was almost unable to move his arms and legs because of joint swelling, pain, and stiffness.

Case 8.—A married woman (the only female in the series), an accountant aged 52, developed pain and swelling of the feet and ankles in November, 1948. A month later her knees became swollen and stiff, and in January, 1949, she noticed that the ends of her fingers were swollen. Five months later she had to stop work because of pain and stiffness in her hands, wrists, and elbows. The only other symptoms at this time were listlessness and "catarrh." In August, 1949, she was admitted to hospital with gastro-enteritis. Generalized osteoarthropathy roused interest, and an *x*-ray film of the chest showed a large circumscribed shadow in the right mid-zone. She was transferred to a thoracic unit in October. By this time she was in poor general condition. She looked old and wizened, with deep facial furrows, marked swelling of joints, and clubbing of fingers and toes. *X*-ray examination showed a massive shadow in the right lower chest and radiological signs of advanced osteoarthropathy. In November she was given a four-day course of nitrogen mustard (total 19 mg.), which produced some relief of joint stiffness. On December 6, as her general condition had improved, a right pneumonectomy was performed with dramatic and immediate relief of her joint pains. Histology of the tumour showed an epidermoid carcinoma. She died six months later with local recurrence of the tumour, but without recurrence of joint symptoms.

Case 10.—A blacksmith aged 59 (the longest survivor) began to have pains in his legs with swelling of the ankles and knees in March, 1947. The following month he could not get out of bed because of joint stiffness. When admitted to hospital in August he had lost 2½ st. (15.9 kg.) in weight. He was investigated as a case of infective rheumatism. The blood sedimentation rate was 65 mm. in the first hour (Westergren). Clubbing of his fingers was noted, and an *x*-ray film showed a round shadow in the apex of the right lower lobe. Bronchoscopy confirmed the presence of an epidermoid carcinoma protruding from the apical segment orifice. He had a right pneumonectomy in September, some six months after the onset of his joint symptoms. The day after operation he was surprised at the relief of pain and joint stiffness and the improvement was progressive. Three weeks after the operation he was walking well. Four months later, *x*-ray examination showed marked diminution in periosteal new bone formation round the radius and ulna (Fig. 3). His progress was uneventful, and he is alive and working more than seven years after the beginning of his symptoms.

Discussion

Although simple clubbing of the fingers is a common phenomenon, true osteoarthropathy is relatively rare, and in this seven-year period we have not witnessed a case related to disease other than lung cancer. As stated recently (*British Medical Journal*, 1954), bronchial carcinoma would seem now to predominate as the chief cause, although Price-Thomas (1953) has stated that no condition is associated with osteoarthropathy as constantly as fibroma of the visceral pleura. This, however, is a rare tumour. It seems possible that many cases of arthropathy previously reported as associated with empyema and lung abscess were suffering from carcinomatous lung abscess or empyema secondary to unrecognized lung cancer.

Mendlowitz (1942), reviewing the "welter of hypotheses" advanced to explain the phenomenon, found them unconvincing. These included the theories of toxaemia, anoxaemia,

capillary stasis, lymph stasis, endocrine disturbance, and autonomic nervous upset. He concluded, however, that increased blood supply must form the cornerstone of any theory of production of osteoarthropathy, and certainly we have found increased peripheral blood flow a constant feature and one which disappears within two or three hours after removal of the lung tumour.

Hypertrophy and hyperplasia from circulatory changes can be observed in arteriovenous fistulae in the limbs. The increased growth of the limb was thought by Sir Thomas Lewis to result from the more rapid flow of blood distal to the arteriovenous shunt. Cross and Wilson (1952) record a case of axillary arteriovenous aneurysm with unilateral clubbing in which increased blood flow to the hand was the only demonstrable circulatory abnormality. Increased peripheral circulation was regarded by Wilson (1952) as an essential feature in acquired clubbing. He demonstrated that blood flow through clubbed fingers was greater than normal, and showed that vasomotor nerves were probably not responsible for this. Lovell (1950) found an excess of fibrous tissue in the distal segments and increase in the calibre of the digital arteries in clubbed fingers. There were abundant characteristic local arteriovenous anastomoses in the distal finger segments, near the junction of the dermis and subcutaneous tissue. He thought that the excess of blood reaching the finger-tip was mainly through these anastomoses and that the by-pass of blood away from the capillary bed might be responsible for the proliferative changes. Mauer (1947), attempting to explain the aetiology of clubbing in both cyanotic and hypervascular states, elaborated this theme. He introduced the interesting concept of peripheral tissue anoxia produced by combination of accelerated peripheral blood flow and raised erythrocyte sedimentation rate; thus erythrocytes, moving rapidly in rouleaux formation through capillaries or arteriovenous shunts, do not have an opportunity for adequate gaseous exchange. It is worthy of note that in our patients both hyperaemia and raised E.S.R. approached normal limits immediately following tumour resection.

The exact mechanism by which increased blood flow produces hypertrophy is unexplained, but from the postulations of Leriche and Policarde (1928) and of Greig (1931) it seems just possible that hyperaemia alone may be the responsible factor in osteoarthropathy. It is acknowledged that new bone is normally restrained by the periosteum, and that a bone cannot exceed its normal limits unless this membrane be removed or raised. Possibly, in this disease, subperiosteal new bone may be deposited as a result of raising of the membrane by serous effusion, an invariable accompaniment of the oedema and cellular proliferation of periosteal hyperaemia. Similar vascular changes may explain the associated subcutaneous tissue and joint involvement. Increase of periarticular circulation modifies synovial fluid both in quantity and in quality and stimulates proliferation of all connective-tissue cells.

Before considering any theory on the mode of production of osteoarthropathy by bronchial carcinoma we must bear in mind the following facts. Osteoarthropathy is produced by only a small proportion of bronchial cancers, most of which are peripheral, grow slowly and concentrically, and show marked central necrosis. There is invariable and immediate relief when such a tumour is resected. Similar relief has been reported to follow ligation of the pulmonary artery on the side of the tumour (Wyburn-Mason 1948) and also denervation of the lung hilum when the tumour could not be removed (Brea, 1948). We have witnessed remission of symptoms occurring spontaneously, following certain drugs, and also after thoracotomy. It must also be remembered that osteoarthropathy can be produced by many other tumours both within and without the thorax. Three hypotheses might be considered.

1. *Tumour affects indirectly the endocrine balance.*—Such a theory is supported slenderly by the production of bone growth and soft-tissue changes in acromegaly and by Selye's work showing that D.C.A. can produce polyarthritis in adrenalectomized animals (Selye *et al.*, 1944). Thomas (1933) described osteoarthropathy occurring after subtotal thyroidectomy. Bariéty and Coury (1950) obtained relief of arthralgia by giving synthetic oestrogen to a patient with inoperable lung cancer. Fried (1943) reported four cases with bronchial carcinoma and osteoarthropathy, all of which showed variable clinical and pathological evidence of endocrine upset. (These changes included an acromegalic appearance, tufting of terminal phalanges, testicular atrophy, hirsutism, macroglossia, and gynaecomastia.) We have already commented on the reversible coarse facial features, and would point out that gynaecomastia (present in two of our patients) must not be accepted as certain evidence of an endocrine aetiology; it has been described in severe starvation and in hepatic cirrhosis, and we have noted it occasionally with bronchial carcinoma in the absence of arthropathy. We have not found testicular atrophy, hirsutism, or macroglossia in our patients. We have not detected any pituitary cortical or thyroid adenomatous changes in the course of three necropsies. Our biochemical investigations lend little support to this endocrine theory, and the dramatic response to removal of the tumour suggests to us a much more direct connexion between the neoplasm and the osteoarthropathy.

2. *Tumour secretes a specific chemical substance, responsible for the change.*—The rapid disappearance of symptoms and signs of osteoarthropathy after tumour resection favours such a theory and also suggests that this substance, possibly of hormonal nature, is destroyed or excreted rapidly. It seems just possible that, excreted in the urine of patients, it might even account for the severe reaction in mice found during our F.S.H. studies. Its effect could be an indirect one through the medium of hyperaemia. On the other hand, the tumour has no special cytological features which would single it out for such a secretory role. A toxic product of tumour necrosis, however, might be absorbed into the blood stream and produce such an effect. While such a theory could explain the relief following pulmonary artery ligation it could not account for the relief after hilar denervation, nor for the occurrence of osteoarthropathy in conditions other than neoplasm.

3. *Theory of an autonomic pulmonary-systemic vascular reflex.*—Cudkowicz and Armstrong (1953a, 1953b) have found precapillary broncho-pulmonary anastomoses in the lungs of patients with variable degrees of finger-clubbing and osteoarthropathy. They were unable to demonstrate such anastomoses in normal lungs or in cases of bronchial carcinoma in which no clubbing was present. The anastomoses in cases of tumour, bronchiectasis, and empyema were seen only in the affected lobes, and there was occlusion of the pulmonary artery proximal to the anastomoses with a variable degree of recanalization. Cockett and Vass (1951) suggest that thrombosis of a pulmonary artery branch may be a stimulus to the development of these anastomoses. Gilroy *et al.* (1951) found arterial blood in the pulmonary arteries of collapsed lobes at operation, strongly suggesting the presence of bronchial arterial blood in the pulmonary circulation. Accompanying this diversion of bronchial artery blood, Cudkowicz and Armstrong demonstrated hyperplasia of the walls and narrowing of the lumina of the smaller peripheral bronchial artery branches, suggesting a state of spasm and reduced function. They suggest that impulses from the peripheral nerve fibres of the lung, rendered ischaemic by the deviation of bronchial arterial blood flow, reflexly influence the formation of the systemic arteriovenous anastomoses in the limbs, described by Lovell. Such an autonomic reflex theory could explain the occurrence of osteoarthropathy in a variety of thoracic lesions, its absence in most lung tumours, and the relief given by tumour removal, pulmonary artery ligation, hilum denervation, and vagus resection (Hansen, 1954).

All three theories have defects, but their further study will probably furnish a conclusive explanation of the syndrome. Investigations by inoculation of animals with

tumour and urine extracts, vascular studies of resected lungs, and autonomic block are all possible keys to the solution of this fascinating problem.

Summary

Bronchial carcinoma may now be regarded as the chief cause of generalized hypertrophic pulmonary osteoarthropathy. A review of 24 patients with this syndrome encountered during the past seven years is presented.

The pathogenesis of osteoarthropathy has been reviewed in the light of our clinical studies, past experimental work, and the dramatic and invariable "cure" effected by tumour removal.

Such patients are often treated for rheumatism or rheumatoid arthritis for many months, and may become bedridden cripples before the presence of a silent lung tumour is suspected.

Fifteen of the patients were submitted to lung resection. Only four are alive. Operative results in this type of tumour might be expected to improve when the significance of such joint symptoms becomes more generally appreciated.

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CARCINOMA OF BRONCHUS IN ASSOCIATION WITH ACTIVE PULMONARY TUBERCULOSIS

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Both pulmonary tuberculosis and carcinoma of the bronchus are common diseases, and it is not a matter of surprise that the two conditions should at times be encountered together. It is generally accepted that there has been, in recent years, an absolute increase in the incidence of bronchial carcinoma, a disease more common in middle-aged and elderly males. With modern methods of treatment, the mortality from pulmonary tuberculosis has shown a dramatic fall, and this implies that more tuberculous patients are surviving into the cancer age. In addition, more cases of active pulmonary tuberculosis are being found in the older men. It is to be expected, therefore, that the two diseases will be encountered more and more in association. For this reason it is of interest to describe the following six cases with the dual pathology. They were all seen during the past three years, the diagnosis being made during life and confirmed at necropsy. They demonstrate the various problems which arise in the diagnosis of these conditions when associated, and their possible interrelationship.

Case 1

A plasterer aged 50 was found, in 1935, to be suffering from bilateral fibrocavernous tuberculosis, the left upper lobe being chiefly affected. He spent two years in a sanatorium, at the end of which time his sputum still contained tubercle bacilli, but his condition was improved. He remained well and at work for the next 10 years in a stable chronic condition. When seen in 1950 he was bothered by a wheezy bronchitis, but for two years there had been no change in the radiological appearances of his lungs, which showed many calcified foci on the right side, while on the left there was some fibrotic disease of the upper lobe.

In October, 1951, he began to deteriorate. There was some staining of the phlegm, be became easily fatigued, but there was little loss of weight. He was forced to give up his work. Radiologically there was a coalescence of the opacities present in the left upper lobe. In February, 1952, streptomycin and P.A.S. were administered to him at home, with little benefit, and in May it was necessary to admit him to hospital. Tomograms of the left upper lung showed a number of large cavities, those lying posteriorly having a fairly regular outline, but there was one anteriorly which had a very irregular wall. This appearance suggested the possibility of a carcinoma having supervened on his chronic pulmonary tuberculosis. He was too ill for bronchoscopy. Despite the administration of further streptomycin, together with isoniazid, his condition deteriorated. In October the sputum still contained tubercle bacilli, but thereafter all sputa were reported as negative for tubercle bacilli on direct smear. Radiologically there was the gradual development of a large dense opacity in the left upper lung, and the left hemidiaphragm became paralysed. No radical therapy was possible, and in March, 1953, he died.

Necropsy revealed the presence of chronic fibrosis and cavity formation of a tuberculous nature in the apices of both lungs, but in the left lung there was also a round necrotic mass (7.5 cm. in diameter), macroscopically a carcinoma, lying mainly in the upper lobe, against the hilum and the aorta.

Histology showed the carcinoma to be of the epidermoid type, arranged in solid masses, with a little differentiation

into squamous cells. The cell type was relatively polymorphic, and the mitotic frequency relatively high. Tubercles were seen in sections from the adjacent portions of the lung.

Case 2

A railway clerk aged 60 was discovered by mass radiography in 1946 to have quiescent tuberculous lesions in both upper lobes. In 1949, however, he developed a cough, and radiographs showed some slight apical fibrosis on the right side, but on the left side there was infiltration in the upper and mid-zones not previously present in 1946. Examinations of the sputum were negative, but Löwenstein culture of one laryngeal swab in October, 1949, revealed a scanty growth of tubercle bacilli. In 1950 tomograms demonstrated a small thick-walled cavity in the left upper lobe. Apart from three months of bed rest, he did not receive any specific treatment, but continued at work feeling fairly well, although he did complain of undue fatigue. In April, 1952, radiographs showed his condition to be stable.

In July he developed a bad "cold," which was followed by stabbing pains in the right axilla, spreading towards the back of the right chest. At this time he had already retired from his work, but he still was very fatigued. He was bothered by considerable dyspepsia, and was losing weight. Radiologically he was found to have developed a new circumscribed homogeneous opacity in the right upper zone. Tomograms showed a well-defined opacity, but there was no central excavation. Sputum tests were negative for tubercle bacilli.

Bronchoscopy was performed, but with negative result. Nevertheless, the presence of a carcinoma was strongly suspected on radiological grounds, but treatment, either by surgery or radiotherapy, was not thought advisable. In January, 1953, he had considerable pain in the right chest and arm and he developed severe headache and vomiting. It was thought that he now had a cerebral metastasis. In April he had to be admitted to hospital. Radiologically the opacity in the right upper lobe had steadily increased in size, but sputum examinations for tubercle bacilli were negative. Later his liver enlarged, he became jaundiced, and he died in August, 1953.

Necropsy revealed an extensive lesion of the right upper lobe, consisting of areas of carcinoma round one division of the right upper lobe bronchus, and a firm plaque of similar appearance under the pleura, both layers of which were firmly adherent. The rest of the right upper lobe was necrotic, with areas suggestive of tuberculosis. The left upper lobe contained fibrocaseous tuberculous disease, with cavitation. There were also scattered firm nodules in both lungs, due to metastases. The liver was enlarged and showed fatty infiltration but no metastases, and examination of the brain failed to show any evidence of secondary deposits.

Histology showed the carcinoma to be of undifferentiated anaplastic type, and there were some foci of tuberculosis adjacent.

Case 3

A painter aged 53 developed in October, 1951, a cough with sputum, associated with fever and loss of weight. When seen in January, 1952, he was found to be in very poor condition, 1½ st. (10 kg.) underweight, with a marked kyphosis and an emphysematous chest. A chest radiograph revealed evidence of tuberculous infiltration and fibrosis in the left upper zone, the right lung being quite clear. Sputum tests were negative for tubercle bacilli. It was significant that a chest radiograph in 1948 had been normal. He spent six weeks in a sanatorium, which he left prematurely at his own request. He was then treated at home with rest and P.A.S. for four months, but with little benefit.

In May, 1952, a new small opacity appeared in the peripheral portion of the right first intercostal space. During the course of the next two years his general condition and the radiological appearance of the lesions in the left apex did not seem to alter, but the opacity in the right upper zone showed a steady increase in size, becoming a large, rounded mass. Sputum tests were negative for tubercle bacilli. The blood Wassermann reaction was negative. His haemoglobin was 87%, and white blood count 13,100 (87% polymorphs).

In June, 1954, his clinical condition deteriorated, and he became more easily dyspnoeic. Bronchoscopy was not attempted, as it was not thought likely that any abnormality would be visible, since the growth, if present, was peripheral. Nevertheless, on clinical and radiological grounds, he was believed to have a carcinoma of the right lung in addition to the quiescent pulmonary tuberculosis in the left lung. Radical therapy was not regarded as being indicated.

In August he developed severe headaches and became mentally confused. He was admitted to hospital, where he was found to have papilloedema, and a cerebral metastasis was suspected. There were now also some subcutaneous nodules under the skin of the right forearm which had not been previously present. He became comatose, and soon died.

Necropsy revealed fibrotic tuberculous lesions in the left apex, adherent to the chest wall, while in the right upper lobe there was a large rounded solid mass of carcinoma (10 cm. in diameter) replacing most of the lobe. The nodules under the skin of the right forearm were confirmed to be secondary deposits. The right cerebellum contained one large metastasis (5 cm. in diameter).

Histology revealed the carcinoma to be of the undifferentiated, polymorphic, large-celled variety. Sections of the left apex showed evidence of fibroid tuberculosis.

Case 4

An unskilled labourer aged 64 developed in January, 1953, a cough associated with undue dyspnoea on effort. He also lost his appetite, had considerable abdominal pain after meals, and was losing weight. In March, 1953, his doctor referred him for a barium-meal examination, but no abnormality was discovered in his alimentary tract. One month later the cough was worse, there was a great deal of offensive yellow sputum, and his voice became husky. He was referred for a chest radiograph, and this revealed a dense opacity in the base of the left upper lobe with central excavation. There was pleural thickening over the left chest wall laterally. In the left lower lobe were miliary changes suggestive of tuberculous disease. He was then admitted to hospital, and the following facts were ascertained regarding his previous history. His mother had died of pulmonary tuberculosis. He himself had had three attacks of "pneumonia" before the age of 35. He had been a regular smoker of 10 cigarettes daily for most of his life.

Examination revealed him to be a very ill wasted man, with marked clubbing of the fingers. There were dullness and bronchial breath sounds, with many rales and rhonchi, on the left side of his chest, and the liver was enlarged. His haemoglobin was 72% and white blood count 16,800 (82% polymorphs). Sputum examinations revealed the presence of tubercle bacilli on direct smear. Pulmonary tuberculosis was diagnosed, but the dense opacity in the base of the left upper lobe made one suspicious of the presence of a carcinoma in addition. Any radical therapy for a carcinoma was, however, quite out of the question. Streptomycin and P.A.S. were administered, but his condition rapidly deteriorated, and he died a fortnight after admission to hospital.

Necropsy revealed the left upper lobe to be a solid mass of carcinoma and cavitation. There was one small focus of carcinoma in the right upper lobe near a bronchus. The left lower lobe presented the appearance of a localized miliary tuberculosis. The liver contained four large metastases (5–7.5 cm. in diameter). On the left side of the neck there was a large mass of glands, and smaller masses were in the anterior mediastinum and around the tail of the pancreas. There was a subcutaneous nodule at the

umbilicus, and scattered enlarged glands in the mesentery, the para-aortic area, and the pelvis.

Histology showed the carcinoma to be small-celled, poorly differentiated to an epithelial character. The cell type was moderately polymorphic, and the mitotic frequency relatively moderate. There were also tubercles distributed throughout the left lower lobe.

Case 5

A bookmaker's clerk aged 45 was seen in January, 1953, with a history of cough and sputum of six months' duration. He had regularly smoked 20 cigarettes daily. For three months he had been feeling increasingly fatigued, and had been running an evening pyrexia—to 99.4° F. (37.4° C.)—and had lost 1½ st. (10 kg.) in weight. His father had died of pulmonary tuberculosis.

On examination he was seen to be very ill, and was mentally confused. There was early clubbing of the fingers, and numerous crepitations could be heard in the left upper lung. A chest radiograph revealed a large cavity in the left upper zone, with infiltration in the left upper and mid-zones. The right lung was normal. It was of interest that a chest radiograph, taken when he was demobilized from the Royal Navy in 1944, was normal. Examination of the sputum revealed tubercle bacilli on direct smear. A diagnosis of active pulmonary tuberculosis was made, and he was admitted to hospital. Treatment with streptomycin and P.A.S. was begun at once, but despite this his condition deteriorated. In May he was bronchoscoped, but, owing to gross upward displacement, the orifice of the left upper lobe bronchus could not be seen. A biopsy was carried out on an enlarged gland in the neck, and histological examination showed the gland to be extensively replaced by an undifferentiated carcinoma, probably squamous-celled. It was now realized that a carcinoma of the lung was present, complicated by pulmonary tuberculosis, but no radical therapy for the carcinoma was feasible.

His condition deteriorated rapidly. He soon became cachectic, and clubbing was more pronounced. Radiologically there was now a larger dense mass in the left upper lung, in which there was a cavity (with fluid levels), the walls of which were very irregular, and in which one could distinguish several nodules of growth. His haemoglobin was 58%, and white blood count 15,200 (87% polymorphs). A right hemiplegia developed, and several epileptiform fits occurred, followed by marked impairment of speech. A skull *x*-ray film showed a small area of thinning of bone in the left frontal area, and it was thought that a cerebral metastasis was present. In July, 1953, he died.

Necropsy revealed a bronchial carcinoma involving and surrounding the left upper and lower bronchi. Distal to this in the lung was a large pus-filled abscess cavity (5 cm. in diameter). There were secondary involved glands in the mediastinum and both sides of the neck, as well as one plaque on the anterior surface of the liver and an enlarged para-aortic gland on the left side. In the brain there was a large cystic area in the left parietal region, the pathology of which was obscure.

Histology showed the lung substance to be infiltrated by cells of a poorly differentiated carcinoma of the bronchus. There were also tuberculous giant cells and endothelial cells.

Case 6

A retired welfare officer aged 69 was seen for the first time in January, 1953. He had suffered from bronchitis for many years, and in 1950 had had a brief attack of left-sided "pleurisy." He had smoked 20 cigarettes daily for most of his life. He had lost weight during the previous three months, and for one month had been having pains in the left chest associated with undue shortness of breath. His cough had become worse, and the phlegm was streaked with blood.

On examination his general condition was very poor and he was markedly dyspnoeic at rest. There was no clubbing of the fingers, but wheezy rhonchi could be heard in both lungs. A chest radiograph revealed some scattered opacities in the right lung, and on the left side there was a dense opacity arising from the hilum and radiating upwards and outwards into the left upper lobe. Examination of the sputum was negative for tubercle bacilli, and the E.S.R. was 56 mm. in the first hour (Westergren). A diagnosis of carcinoma of the bronchus was made, but further investigation by bronchoscopy was not carried out, in view of his age and very poor condition.

In March he was admitted to hospital. He was cachectic, with an irregular pyrexia—to 102° F. (38.9° C.)—and had now developed clubbing of the fingers. Examination of the chest revealed diminished movement and air entry on the left side, and the coin test was positive. A radiograph revealed that a spontaneous pyopneumothorax had taken place on the left side. The sputum contained scanty tubercle bacilli on direct smear. The haemoglobin was 70%, and the white blood count 17,300 (81% polymorphs). The left chest was aspirated and turbid yellowish-green fluid withdrawn. This was lymphocytic and no tubercle bacilli were seen on direct smear, but Löwenstein culture proved positive. It was realized that the carcinoma was now accompanied by a tuberculous pyopneumothorax, but no radical therapy would avail. He deteriorated rapidly, and died in May, 1953.

Necropsy revealed the left lung to be a solid mass of cancer and abscesses, and perhaps tubercle, too. The left hilar glands were replaced by cancer. The neoplastic left lung had spread over the mediastinum, but the glands themselves were not obviously invaded, apart from the hilar ones. The left pleural cavity contained some purulent fluid, and the right upper lobe showed miliary tuberculosis.

Histology showed a bronchogenic carcinoma with solid epithelial alveoli but no further epidermoid differentiation. The cell type was fairly regular and the mitotic frequency relatively low. There were also scanty tuberculous follicles.

Discussion

It is now nearly 150 years since Bayle (1810), the great teacher of Laennec, described the "phthisies cancéreuses," but he used the term "phthisis" to include the wasting which might ensue from any pulmonary disease, and it is doubtful whether he was in fact describing tuberculosis and carcinoma occurring together in the lungs. Credit for the first description of the two diseases coexisting must be given to Penard (1846). In recent years it has become increasingly recognized that carcinoma and tuberculosis may occur together in the lungs, and reports have been published on the subject (Fried, 1935; Cohen, 1949; Blasi, 1950; Shefts and Hentel, 1950; Couts, 1951; Helm and Moon, 1952; Nuessle, 1953).

Incidence

The incidence of the association of the two diseases at necropsy has varied greatly in the large series published by different authorities, and is shown in Tables I and II. Among live patients, Källquist (1952) has described a series of 5,527 cases of pulmonary tuberculosis, of which 11 (0.2%) had carcinoma of the bronchus as well; and Seyfarth (1952), in a series of 1,103 cases of carcinoma of the lung, found 11.42% to have evidence of tuberculosis also.

The discrepancies between these different series may partly be explained by the varied interpretations adopted

TABLE I

Authority	Necropsies on Pulmonary Tuberculosis	Coincident Carcinoma
Gerstl *et al.* (1946)	1,600	0·44%
Drymalski and Sweany (1948) ..	2,000	0·75%

TABLE II

Authority	Necropsies on Carcinoma of Lung	Coincident Active Tuberculosis
Farber *et al.* (1949)	266	3·8%
Bryson and Spencer (1951) ..	866	1·8%
Gloyne (1951)	648	5·5%

by the different workers regarding what constituted tuberculous disease. Thus Bryson and Spencer's (1951) low figures included only those with chronic active pulmonary tuberculosis, as distinct from mere microscopical evidence of old chronic tuberculous lesions.

It may be concluded that the incidence of active tuberculous changes in patients suffering from cancer of the lung (as exemplified in Cases 4, 5, and 6) are not rare, while patients with pulmonary tuberculosis developing a new growth (as in Cases 1, 2, and 3) are less common.

Problems of Diagnosis

When a carcinoma of the bronchus develops insidiously in a known case of chronic pulmonary tuberculosis (as in Cases 1, 2, and 3), the diagnosis of the dual pathology is likely to be more difficult than when a diagnosed case of carcinoma of the bronchus is complicated by the finding of tubercle bacilli in the sputum (as in Cases 4, 5, and 6).

Clinically, carcinoma of the bronchus should be suspected in a man over the age of 40, usually a smoker, and known to have chronic pulmonary tuberculosis, who appears to be more ill than his tuberculous condition alone warrants, or if he is unusually dyspnoeic or has a pain in the chest which is persistent. It is of interest that in the six cases described above, haemoptysis was not a conspicuous feature. Another suspicious feature is the failure to respond to specific antituberculous chemotherapy. There may, of course, be many reasons for this, but one of them may be the complication of a carcinoma of the bronchus. Similarly, excessive anaemia and a polymorphonuclear leucocytosis (as in Cases 3, 4, 5, and 6) may indicate the presence of a carcinoma superimposed on the tubercle.

The radiological features suggestive of carcinoma are the superimposition on the tuberculous changes of a dense opacity, especially near the hilum. Enlargement of hilar glands, paralysis of a hemidiaphragm, and erosion of a rib are also helpful diagnostic signs. Where there is a thick-walled cavity with a very coarse irregular lining (often best seen in tomograms), it may merely mean a breaking-down neoplasm, but it may also indicate a cancerous development in a tuberculous cavity (as in Case 1).

Bronchoscopy (which was possible only in Cases 2 and 5) did not prove at all helpful. The diagnosis of a cerebral secondary deposit, or the biopsy of an enlarged gland (as in Case 5) or of a subcutaneous nodule (as in Case 3), may be conclusive, but it indicates that such a metastasis precludes any hope of a radical cure.

So long as it is remembered that carcinoma and tubercle in the lung do not exclude one another, it is very unlikely that the diagnosis of the two conditions occurring together will prove difficult or be unduly delayed. In a known case of pulmonary tuberculosis the early diagnosis of a superimposed carcinoma is of great importance, since otherwise it may prove too late to treat. Although the six cases described here were diagnosed correctly during life, the carcinoma was too advanced in all of them to allow any radical therapy to be considered. It should be remembered that the finding of tubercle bacilli in a case of carcinoma of the bronchus may be of minor importance so far as the practical management of the case is concerned. The treatment of the cancer takes precedence.

Relationship of the Two Diseases

The association of tuberculosis and carcinoma of the lung may be considered in various ways.

1. *The Two Diseases Exert a Mutual Antagonism.*—Rokitansky (1854), as a result of his famous morbid anatomical studies, first propounded the theory that there was an antagonism between cancer and tuberculosis, and this was supported by Raymond Pearl (1929) in his statistical studies based on the records of the Johns Hopkins Hospital. Cooper (1932), however, in his comprehensive study of the association of the two diseases, showed conclusively that the two diseases were not antagonistic.

2. *Tuberculosis (active or healed) is a Factor in the Production of Carcinoma.*—Cherry (1931), as a result of experiments on mice and his statistical studies, believed that cancer was predisposed to by previous tuberculous disease. Woodruff and Nahas (1951), analysing 23 cases of carcinoma of the bronchus, found 12 which were squamous-celled, and these were associated with large calcified foci in the same lobe or adjacent tracheo-bronchial lymph node, but not with active tuberculous disease. They suggested that it was healed tuberculosis which, leading to calcification and bronchiectasis (usually saccular, in the upper lobes), predisposed to the development of cancer, since smoking tended to produce an accumulation of tobacco products in the saccules. It has been thought by many that chronic irritation and atypical regeneration of epithelial tissues in old tuberculous cavities may lead to neoplastic changes. Bryson and Spencer (1951), however, found in the 866 cases of cancer of the lung they studied *post mortem* only four examples where the cancer arose in the wall of a bronchiectatic cavity.

3. *Cancer Activates Pre-existing Tuberculous Disease.*—When one considers the frequency of healed tuberculous foci in the lungs it is not surprising that carcinomatous infiltration into the lung, as well as the debility produced by the cancer, should lead to erosion of the tuberculous foci, with proliferation of the tubercle bacilli and reactivation of the tuberculous disease. Thus Pagel (1934) showed that a cancer nodule in the lung may be seen to be encircled by recent macroscopic tuberculous foci. Even if a very small lesion is eroded by growth, some tubercle bacilli may be found in the sputum, but this may be of minor importance (Gloyne, 1951).

It is very likely that either of the points of view described in (2) and (3) above may operate in different circumstances. It is also true, however, that in many cases the two diseases arise quite independently, running their separate courses with little effect on each other.

Summary

Six cases in which carcinoma of the bronchus and active pulmonary tuberculosis were associated in male patients over the age of 40 are described. In three a carcinoma developed insidiously in known cases of chronic pulmonary tuberculosis. In the other three, carcinoma of the bronchus was complicated by the presence of active pulmonary tuberculosis.

The interrelationship of the two diseases and the problems of their diagnosis are discussed.

The incidence of the two diseases occurring together is presented, and it is suggested that possibly this association will now be encountered more frequently.

I should like to thank Dr. C. O. Edwards for allowing me to quote Case 2, and Dr. J. C. Lees for giving me access to his necropsy records.

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ACQUIRED ICHTHYOSIS IN HODGKIN'S DISEASE

BY

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Involvement of the skin by either specific or non-specific lesions is a common finding in Hodgkin's disease. In a study of 156 cases Epstein and MacEachern (1937) found that 53.2% showed skin changes. A rare and interesting change is that of acquired ichthyosiform atrophy. It simulates congenital xerodermia so closely that it can be overlooked unless it is appreciated that the eruption has not been present since infancy. Ronchese (1943) first described the onset of an ichthyosiform atrophy of the skin in a patient with Hodgkin's disease eleven months before the patient's death and while he was apparently in good health. Since then Glazebrook and Tomaszewski (1944, 1947) have reported the skin change in association with cases of Hodgkin's disease and lymphosarcoma, Welch and Epstein (1952) in a case of Hodgkin's disease, and Forman (1953) in a case of reticulosarcoma. It is probable that the complication occurs more frequently than the scanty reports suggest, as it was present in the four following cases.

Case 1

A man aged 48, a steelworks gas-producer, some five months before admission began to feel weak and ill, and complained of a pain in the right loin which spread round to the abdomen. He vomited occasionally and was troubled with morning diarrhoea, sometimes three to four loose stools after rising. There had been a weight loss of several stones in the preceding year. On several occasions in the preceding months he had been confined to bed with attacks of so-called "flu." For two months before admission to hospital he noticed that his skin had become dry and scaly (Fig. 1) but not irritable. He was adamant that he had never had a skin abnormality before this.

On examination he appeared wasted, and the skin of the whole body and face showed a dry ichthyotic change. The ichthyosis was indistinguishable from a congenital ichthyosis, though at the time no special attention was paid to whether it spared the flexures. Enlarged glands were detected in the left supraclavicular region and in the left axilla. The spleen was enlarged a handbreadth below the costal margin. Gland biopsy showed Hodgkin's disease. Histological examination of the skin showed only hyperkeratosis and atrophy. There was no sign of an infiltrate. Dark-adaptation tests gave results within normal limits.

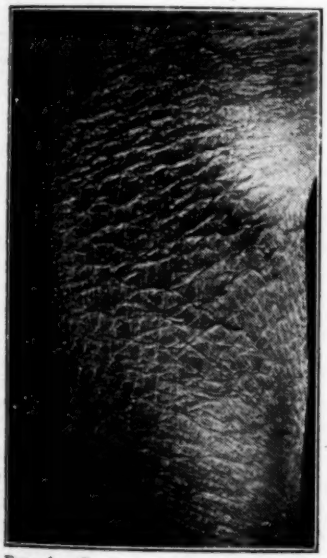

FIG. 1.—Case 1. Showing well-marked ichthyosiform change in the skin of the arm.

The patient was included in the M.R.C. trial of R.48 and at first seemed to benefit from treatment, the glands and spleen diminishing in size. Coincident with this improvement the ichthyosis became less pronounced.

Five months later he was readmitted for transfusion, and his ichthyosis was then worse than it had been originally. He was readmitted on several occasions in the next two years, but contact with him was eventually lost. He is presumed to be dead.

Case 2

In August, 1953, I was asked to see a 52-year-old man in the Sheffield Royal Hospital, under the care of Dr. T. E. Gumpert. He had been admitted six days previously with a five-weeks history of severe diarrhoea, which had come on suddenly when on holiday in Germany and which had not been controlled with sulphaguanidine. For several weeks previous to the onset of diarrhoea he had felt listless and tired. Soon after the start of the diarrhoea the skin of his face felt tight and drawn and the skin of his body became dry and scaly.

On examination the skin of the chest and trunk was dry, was slightly erythematous, and showed large leafy scales; the facial skin seemed to be tightly stretched and was desquamating. On the limbs the appearance was identical with a moderate degree of congenital ichthyosis, though there was no sparing of the flexures. No enlarged lymphatic glands were found, or any abnormality on palpation of the abdomen.

At this stage the tentative diagnosis was a chronic dysenteric infection, and the skin change was ascribed to dehydration. Culture of stools, however, revealed no pathogens, and agglutinations were negative for salmonella. Sigmoidoscopy revealed only inflamed and oedematous mucosa, and a barium enema gave normal results. A blood count showed: Hb, 68%; red cells, 3,200,000; white cells, 4,400 (normal differential); platelets, 32,000. Marrow examination was inconclusive. The only other really positive finding was some enlargement of the hilar glands seen on a chest *x*-ray film and tomogram.

The course of the illness was one of uninterrupted deterioration. The haemoglobin and platelets fell, and extensive purpura developed shortly before the patient died, one month after admission. A tentative diagnosis of Hodgkin's disease, based on the ichthyotic skin change, the discovery of the enlarged hilar glands, and the course of the illness, was reached before his death.

Necropsy.—The relevant findings were enlargement of the glands at the base of the neck and in the mediastinum. These showed a grey uniform cut surface and were rather soft. The lungs and bronchi were not involved. Many whitish nodules were present in the omentum, which was almost devoid of fat; in the wall of the jejunum and in the wall of the ileum were firm masses made up of nodules aggregated together. They were firmer and more rubbery than the mediastinal glands. The aortic glands, and particularly those in the portal fissure and around the pancreas, were enlarged and firm. The liver showed a whitish mottling and at one point appeared to be infiltrated. The spleen was small and fibrotic. On macroscopic examination there was still some doubt about the nature of the nodules in the jejunum and ileum, which resembled carcinomata. Histological examination showed that there were deposits of sclerosing Hodgkin's disease in all coats of the bowel. The lymph nodes from the portal fissure, and the liver and spleen, showed recognizable Hodgkin's disease. The mediastinal nodes were less characteristic, and in some areas resembled an undifferentiated malignant neoplasm. The pathologist, Dr. J. L. Edwards, was confident, however, that only one pathological condition was present—Hodgkin's disease. Section of the skin showed similar findings to the first case—hyperkeratosis, with atrophy of the remainder of the skin elements and no evidence of infiltration in the dermis.

Case 3

An old-age pensioner of 67 had suffered for two years from an eczematous eruption on the feet and ankles. Some four months before he attended hospital he had developed hard painless lumps on the skin of the shoulders and chest. He had not lost weight nor did he feel unwell.

On examination a well-marked ichthyosiform change was present on the skin of the face, trunk, and limbs. This did not spare the flexures. He was uncertain how long the dry scaliness had been present, but was sure it was of recent onset. Multiple skin tumours of firm consistency and a reddish-purple colour, varying in size from a pea to a golf ball, were present over the shoulders, chest, upper abdomen, and thighs. Enlarged glands were found in the neck and the supraclavicular axillary and inguinal regions. The liver and spleen were not palpable. Skiagrams of the chest showed no mediastinal glands. Marrow puncture and blood count revealed no abnormality.

FIG. 2.—Case 3. Showing multiple skin tumours on the trunk.

In view of the ichthyotic change, the nodules were presumed to be due to Hodgkin's disease rather than secondary carcinomata, and this was substantiated by the histological findings of a reticulosarcoma of Hodgkin's type.

Case 4

An 85-year-old woman complained of painless lumps appearing on the back of her neck some two months previously. After discovering those lumps she had noticed others on the trunk.

Examination showed a dusky-red nodular tumour on the back of her neck and another below her left ear. Less obvious smaller nodules were present over the left parotid region and the trunk. No enlarged lymph nodes were found. nor was there demonstrable enlargement of liver and spleen. On the trunk was a mild generalized ichthyosis which she said was of recent onset. The nodules were obviously either secondary carcinomatous deposits or some form of reticulosis. The presence of the ichthyosis suggested the likelihood of the latter, and histological examination of a neck nodule showed a reticulosis of mycosis fungoides type. The nodules failed to respond to radiotherapy or triethylene melamine, and she died two months after admission to hospital.

The significant findings at necropsy were nodular plaques of greyish-white tissue on the lateral thoracic wall and on the lung beneath the pleura. The mediastinal lymph nodes were enlarged. More neoplastic nodules were present on the peritoneal surface of the small and large intestine and in the tail of the pancreas, and the mesenteric lymph nodes were massed together and enlarged. Another greyish-white mass was seen to surround the pelvis, ureter, and inferior pole of the right kidney, and more were present on the posterior wall of the uterus and in the broad ligaments. The liver and spleen showed no macroscopic change. Sections from the affected organs showed deposits of large pleomorphic neoplastic cells characteristic of a reticulosarcoma.

Discussion

In the present series of cases no light has been thrown on the mechanism of production of this curious skin change, but it seems probable that it falls into the group of non-specific skin changes, a great variety of which are known to occur in Hodgkin's disease and allied reticuloses.

In Case 1 the ichthyosis did improve during a remission of the Hodgkin's disease whilst under treatment with R.48, and this suggests a close association between the presence of Hodgkin's tissue and the skin change. Similar improvement was reported by Welch and Epstein when their patient was given *x*-ray therapy. Vitamin A was being given at the same time, so there is also a possibility that this played some part in the improvement. A disorder of vitamin A metabolism due to liver damage was suggested by Glazebrooke and Tomaszewski as the cause of ichthyosis, but in Forman's case blood vitamin A studies were normal, and in my Case 1 dark-adaptation tests were normal.

If the ichthyotic change were due to liver damage alone one would expect to find it in other types of severe liver disease, and such is not the case. Also, it does not occur in association with secondary carcinomatous damage to the liver.

The onset of the ichthyotic change occurs early in the course of the disease and before there has been any appreciable wasting, so that mere inanition is not the cause.

From a practical point of view acquired ichthyosiform atrophy is a rare change, but it may be of value when the diagnosis of Hodgkin's disease is in doubt, as in Case 2. It is not easily differentiated from congenital ichthyosis, though my impression is that the acquired type affects the trunk and face more than the limbs, and, also, it does sometimes involve the flexures, which are usually spared in the congenital variety. Histologically there is no difference.

The onset of an ichthyotic eruption in an adult should certainly initiate a search for an underlying lymphoblastoma.

Summary

Four cases of an acquired ichthyosis associated with Hodgkin's disease and reticulosarcoma are described. The importance of investigating cases of acquired ichthyosis for underlying Hodgkin's disease or lymphoblastoma is stressed.

I should like to thank Professor C. H. Stuart-Harris and Dr. T. E. Gumpert for allowing me to report their cases, Drs. J. L. Edwards and L. C. D. Hermitte for the post-mortem reports and histological findings, and Mr. Brookes for the photographs.

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The Victoria Cross awarded to Surgeon-Major Edmund Baron Hartley in 1879 was acquired for the record sum of £300 by the Royal Army Medical Corps when it came up for auction in London on March 17. Hartley, the son of a Devonshire doctor, was born in 1847 and qualified from St. George's Hospital in 1874. He then became district surgeon in Basutoland. In 1877 he joined the Cape Mounted Rifles as surgeon, becoming principal medical officer in the following year, and subsequently colonel in command of the Cape Medical Corps. He served in several campaigns during the Zulu war of 1877–9, and in the Boer War. He was decorated with the Victoria Cross for the conspicuous gallantry he displayed on June 5, 1879, in attending the wounded under fire at the unsuccessful attack on Morosi's Mountain, Basutoland. Other awards to Hartley included in the sale were the Cape General Service Medal with three bars (only thirteen other recipients of this medal and three bars are known), the Queen's South Africa Medal with three bars, and the King's South Africa Medal with two bars. He was appointed C.M.G. in 1900; he died on March 20, 1919, in his seventy-second year.

FOETAL FIBROELASTOSIS

BY

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Interest has been aroused from time to time in a cardiac lesion found in infants, the main features of which are thickening and opacity of the lining of the left chambers of the heart. First described as foetal endocarditis in the nineteenth century, it has subsequently been called congenital endocardial sclerosis (Craig, 1949), endocardial dysplasia (Prior and Wyatt, 1950), and endocardial sclerosis (Bonham-Carter *et al.*, 1952), and is now most generally known as fibroelastosis (Weinberg and Himelfarb, 1943). These titles reflect to some extent the changing conceptions of an aetiology which, however, has never been satisfactorily settled.

Recently a disease similar, superficially at least, to fibroelastosis in infancy has been described by several authors, including Bedford and Konstam (1946), Ball *et al.* (1954), and O'Brien (1954). This has occurred predominantly in natives of the Middle East area, and is characterized *post mortem* by cardiac enlargement and sclerosis of the endocardium; the possibility that the one may be a late stage of the other has naturally been raised. Already cases previously known as idiopathic cardiac hypertrophy of infancy, in which endocardial thickening may occur, have been linked with fibroelastosis, and this attempt to widen the scope of the disease to embrace all cases showing endocardial sclerosis is attractive. The examination of this problem has been prompted by the occurrence in the last two years in the Brighton Group of Hospitals of three examples of congenital aortic stenosis accompanied by fibroelastosis of the endocardium.

Case 1

Maternal History.—Aged 27 and in good health; W.R. negative; Group O, Rh positive. She had two healthy children, aged 4 and 7 years; there have been no abortions. Study of the antenatal records and retrospective questioning revealed no illness during the pregnancy; the parents were not blood relations.

The infant, a male, weighed 8 lb. 10 oz. (3.9 kg.) at birth. Labour was spontaneous and easy, and his immediate recovery was good. On the first day he was observed to be somewhat cyanotic at times, and subsequently respiration became laboured and rapid with frequent cyanotic attacks, in one of which, on the fourth day, he died. No abnormal physical signs had been found during life.

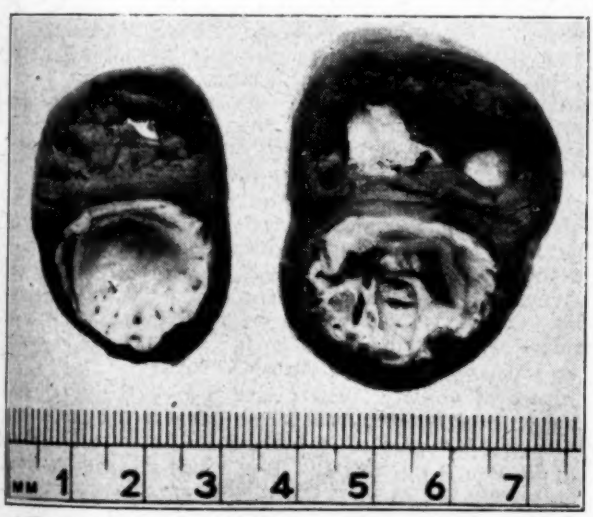

FIG. 1.—Horizontal section through the ventricles. Case 1.

Necropsy.—Complete examination revealed severe venous congestion; apart from the changes in the heart no developmental or pathological lesion was found.

Heart (Fig. 1).—Weight 25.5 g. Size, apex to base, 4.5 cm.; side to side, 5 cm.; antero-posterior, 3.5 cm. The interventricular groove on the anterior surface ended 0.5 cm. above the apex, which was thus formed from the myocardium of the right ventricle. The right atrium and ventricle were dilated and the latter was also hypertrophied (wall 0.5 cm. thick). The left atrium was normal in size and the left ventricle small. The inner lining of the left ventricle was yellow, tough, and opaque; it measured 0.5 cm. over the interventricular septum and 0.4 cm. elsewhere. The foramen ovale was patent but capable of being closed by a flap-like valve of endocardium. The ductus arteriosus was widely patent and slightly larger than the aorta in diameter. The mitral, tricuspid, and pulmonary valves were natural. The aortic valve was stenosed by fusion of the contiguous borders of the valve cusps, except for a narrow slit between the anterior and left posterior ones.

Case 2

Maternal History.—Aged 27 and in good health; W.R. negative; Group O, Rh positive; no immune antibodies in the serum. She had one child, aged 3½ years, who was healthy, and there had been no abortions. Study of the antenatal records and retrospective questioning revealed no illness during the pregnancy. The parents were not blood relations.

The infant was female and weighed 5 lb. 7 oz. (2.5 kg.) at birth. Born spontaneously, she appeared well until 2 days old, when she became temporarily dusky in colour and thenceforward suffered from cyanotic attacks; in one of these, on the fifth day, she died. No abnormal physical signs had been detected during life.

Necropsy.—There was extreme generalized venous congestion; apart from this, complete examination revealed no congenital or pathological lesion except in the heart.

Heart.—Weight 22.5 g. Size, apex to base, 4.5 cm.; side to side, 4 cm.; antero-posterior, 3.5 cm. The interventricular groove on the anterior surface of the heart ended 1.5 cm. above the apex of the heart, which was thus formed by the myocardium of the right ventricle. The right atrium was dilated, the right ventricle dilated and hypertrophied (wall 4 mm. thick); the left atrium was small and the left ventricle vestigial. The endocardium of the left ventricle was tough, yellow, and thickened, especially over the interventricular septum, where it varied from 2 to 3 mm. in thickness. The ductus arteriosus was widely patent and a little larger than the arch of the aorta in diameter. The foramen ovale was patent, but could be closed by an efficient valve-like fold of endocardium. The tricuspid, pulmonary, and mitral valves were natural. The aortic valve was stenosed by fusion of the contiguous borders of the valve cusps, except for a narrow slit between the anterior and left posterior ones; there was no fibrosis or distortion of the cusps, which remained thin and pliable. The coronary arteries were normal in origin, structure, and distribution.

Case 3

Maternal History.—Aged 20 and in good health; W.R. negative; Group O, Rh negative, with no immune antibodies in the serum. She had had no previous children, abortions, or blood transfusions. Retrospective questioning and perusal of the antenatal records revealed no illness during the pregnancy. The parents were not blood relations.

The infant, a male, weighed 5 lb. 12 oz. (2.6 kg.) at birth; blood Group O, Rh positive. Hb at birth 16.3 g. per 100 ml., direct Race–Coombs test negative. The day after birth he was observed to be dusky-coloured at times.

Cyanotic attacks thereafter became frequent, and on the eighth day he died in one of them. No abnormal physical signs had been detected during life.

Necropsy.—There was severe systemic venous congestion, but apart from this no congenital or pathological lesion was found other than that of the heart.

Heart.—Weight 17.3 g. Size, apex to base, 4.4 cm.; side to side, 4 cm.; antero-posterior, 3.4 cm. The interventricular groove on the anterior surface ended 1.6 cm. from the apex of the heart, which was formed by the myocardium of the right ventricle. The right atrium was dilated, the right ventricle dilated and hypertrophied (wall 4 mm. thick). The left atrium was small and the left ventricle vestigial. The lining of the left ventricle was opaque, tough, and yellow-white, especially over the interventricular septum, where it was 3 mm. thick. The columnae carneae were absent. The foramen ovale was widely patent, but could be closed by a flap-like valve of endocardium. The arrangement of the great vessels is shown in Fig. 2. The ductus arteriosus was patent, 6 mm. in diameter, and the same size as the arch of the aorta. The ascending aorta was 2 mm. only in diameter and there was no communication between it and the left ventricle. The aortic valve was closed by complete fusion of the valve-cusp borders. It was 2 mm. in diameter, and when viewed from the aortic side presented three distinct pits defined by three ridges meeting at the centre and corresponding to the edges of the aortic valve cusps. The coronary arteries arose opposite the anterior and left posterior depressions and were distributed normally; they were fed by retrograde blood-flow down the ascending aorta, which served no other purpose. The tricuspid and pulmonary valves were natural, the mitral small but not stenosed.

FIG. 2.—Arrangement of the great vessels in Case 3.

Microscopy

Sections were taken from the myocardium, opaque endocardium, aortic valve cusps, and coronary arteries in each case: the microscopical appearances were similar in all, so that their description may be combined.

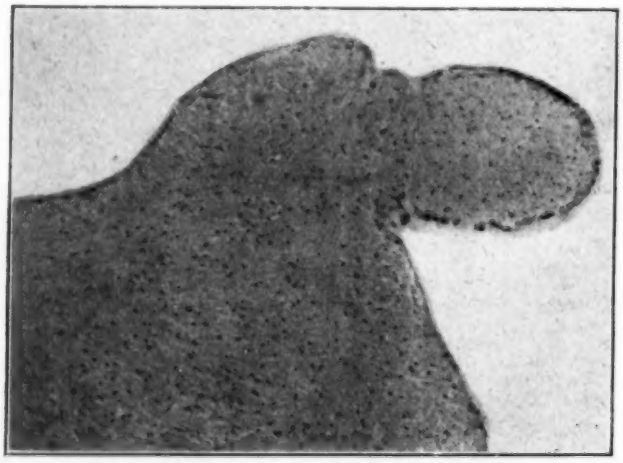

FIG. 3.—Section at point of fusion of an aortic valve cusp. (×95.)

Section of the coronary arteries taken at 0.5-mm. intervals revealed no constriction of lumen or abnormality of the wall. The aortic valve cusps showed some increase in volume, made up by interlacing bundles of collagen undergoing oedematous change. In no case was there inflammatory cell infiltration; in particular, section at the point of fusion of valve cusps (Fig. 3) showed no scar tissue.

The myocardium was normal, with no inflammatory cell aggregates or fibrosis. The junction between the myocardium and the opaque endocardium was irregular and ill-defined, and in places islands of myocardial fibres were surrounded by tongues of fibrous tissue (Fig. 4). Many of the myocardial fibres were degenerate in the junctional layer and were being replaced by fibroblasts. The bulk of the opaque endocardium was composed of normal collagen fibres, but when stained with orcein and eosin a high proportion of elastic fibres were found. A feature of the junctional layer was a large number of thin-walled dilated blood vessels.

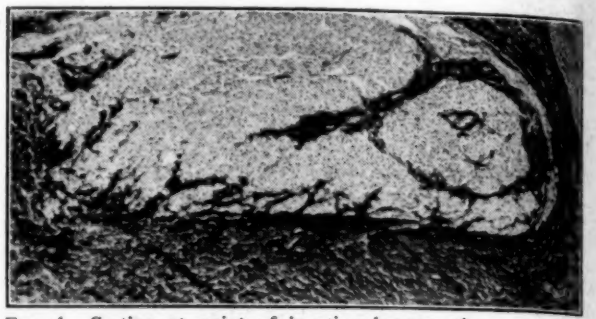

FIG. 4.—Section at point of junction between the myocardium and the endocardium. (×55.)

Discussion

Aortic atresia is a rare condition. Canton (1948-9) appears to have been the first to report a case, and since then 20 others have been traced—those of Shattock (1881), Summons (1906), Gauss (1916), Fraser (1921), Mueller (1924), Abbott (*Loose-Leaf Medicine*), Schrader (1928), Philpott (1928), Willer and Beck (1932) two cases, Bellet and Gouley (1932), Farber and Hubbard (1933), Wesson and Beaver (1935), Roberts (1936), Rossman (1942), Craig (1949) four cases, and Halliday (1954). Case 3 reported here is thus the 22nd recorded example. In addition to aortic atresia, all showed a hypoplastic left ventricle lined by an opaque, white, thickened endocardium with an intact interventricular septum. The appearance of the aortic atresia is striking, and descriptions exactly similar to that given in Case 3 are repeatedly encountered. It is evident that the valve cusps have developed regularly and then fused along their borders, for, macroscopically, there is usually no distortion of pattern and microscopically no evidence of fibrosis. Incomplete aortic stenosis such as was found in Cases 1 and 2 differs from that of complete atresia in degree but not in essential nature. Fusion of valve cusps occurs as in atresia, except that a slit may be left between one pair, while endocardial sclerosis is constant and hypoplasia of the left ventricle is usually found. It seems likely that atresia and stenosis are both the end-result of the same disease process.

The clinical pattern of aortic atresia is very constant. The infant recovers satisfactorily from the immediate stress of parturition and then suffers from cyanosis and difficult respiration 12–36 hours after birth. Usually no abnormal physical signs are elicited and death occurs at about 5 days old. Out of the 22 recorded examples, 14 died in less than 6 days, while, of the remainder in which the age at death was given, only 3 lived more than 15 days.

Cases of aortic stenosis pursue a very similar clinical course, and it is exceptional for an infant to live more than 14 days. The cases of Farber and Hubbard (1933) and of Du Shane and Edwards (1954), in which the patients lived for 9 weeks and 2½ years respectively, are very exceptional, but both appeared to have had typically fused valve cusps.

Recent literature on fibroelastosis gives the impression that this change may occur at any age from birth to 5–6 years of age, and that valvular stenosis may or may not be associated in any particular example. However, study of available case reports and photographs shows that the occurrence of aortic stenosis is by no means haphazard. The heart weights and times of death when stated in all the patients under 9 months old accepted by Gowing (1953) in a recent review of the subject are arranged in Fig. 5; added to these are

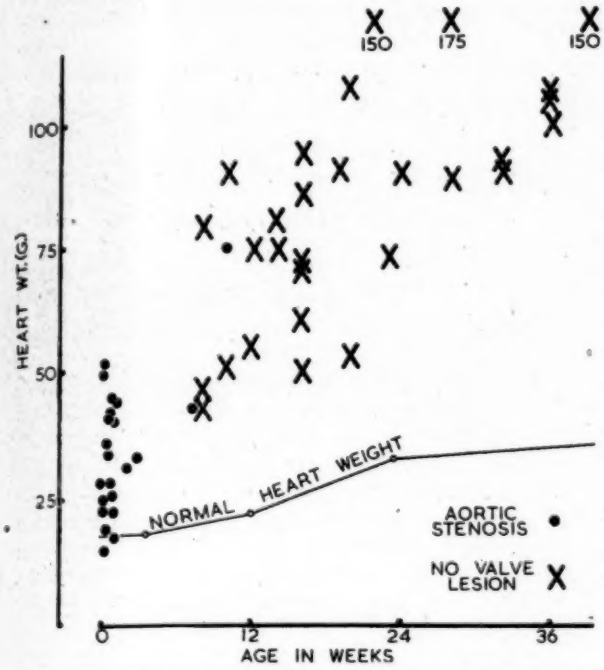

FIG. 5.—Cases of foetal and infantile fibroelastosis contrasted.

all cases of aortic stenosis or atresia which could be traced. It is apparent from this that fibroelastosis in infancy is capable of division into two groups which are in many ways contrasted.

One group, which is referred to as foetal fibroelastosis and which is represented by the three cases described in this paper, is characterized by aortic stenosis (sometimes accompanied by mitral stenosis), early death, and relative or absolute hypoplasia of the left ventricle; the heart weight is only moderately increased and is accounted for by right ventricular hypertrophy. The other group, many cases of which had been described previously as idiopathic cardiac hypertrophy of infancy, is without valvular lesions and is referred to as infantile fibroelastosis. The left ventricle is grossly hypertrophied and usually dilated, and it accounts for heart weights three to five times the normal; death is uncommon under 3 months old, and it is interesting that fibroelastosis without valvular stenosis has not been recorded at birth except in the case described by Prior and Wyatt (1950). The latter would be an interesting exception, but, since it is given no separate description and there is no photograph, it is of doubtful value. Fibroelastosis of the endocardium is common to both groups, but the gross thickening found in foetal cases is seldom seen in infantile fibroelastosis: in some of the descriptions and photographs of the latter it is so slight that it raises the question of how far the term should be stretched.

Aetiology

Gross (1941) effectively rejected intrauterine inflammation as an explanation for the changes found in foetal fibroelastosis. Subsequently maternal infection and mesenchymal dysplasia have been popular hypotheses, but neither has evidence to support it. However, the microscopical appearances have many features in common with those found in endocardial fibrosis overlying adult cardiac infarction. The irregular junctional line and dilated vessels, the occasional report of lymphocytic aggregates and calcification, and the evident fibrous replacement of the myocardial fibres bordering the endocardium are all similar and suggest that anoxia may be common to both. The main difference between the two is lack of fibrosis in the myocardium outside the junctional layer in foetal fibroelastosis. An explanation of this may lie in the way in which the anoxia is caused.

For a considerable time *in utero*, until the coronary circulation is fully established, the foetal heart is dependent for nourishment on blood flowing through its cavities. During this period temporary closure of the foramen ovale during the course of its development, along the lines suggested by Johnson (1952), would prevent oxygenated blood in the right atrium from flowing into the left atrium and left ventricle, and this may cause degeneration of the endocardium covering the aortic or mitral valves. In the absence of sufficient blood flow to keep them apart, fusion of the raw edges of the cusps would be expected with little fibrosis or distortion. If aortic stenosis was established in this way, stenosis and consequent anoxia of the blood in the left ventricle would occur and lead to degeneration of the layer of myocardium lining the cavity and the development of the fibrosis found in foetal fibroelastosis. Naturally, the myocardium outside the area supplied from within the cavity would be unaffected and normal in appearance. All the changes found in foetal fibroelastosis would thus be explained.

Support for this hypothesis is found in the rare examples of aortic and mitral atresia accompanied by ventricular septal defects. For example, Dolgopol (1934) described a heart with aortic atresia in which the vestigial left ventricle communicated with the right through a narrow slit: the left ventricular cavity was lined by normal endothelium. One of Halliday's (1954) cases showed mitral atresia and multiple ventricular septal defects. Fibroelastosis was found in the left atrium but not in the left ventricle. If both aortic stenosis and fibroelastosis were the result of mesenchymal dysplasia the presence of an interventricular septal defect would not influence the development of the latter. On the other hand, if fibroelastosis is the result of stasis and anoxia of blood in the left ventricle the change would not occur if oxygenated blood were available from the right ventricle through a septal defect. In fact, no case of aortic atresia has been traced in which fibroelastosis has occurred accompanied by an interventricular defect, and, conversely, no case of aortic atresia with an intact interventricular septum was without fibroelastosis.

Detailed discussion of the aetiology of infantile fibroelastosis does not come within the scope of this paper. However, the rarity of its occurrence within the first two months of life makes a developmental defect of embryonic origin unlikely, and an explanation bringing it into line on the basis of anoxia may be found with further research.

A connexion between cases of foetal fibroelastosis and the group described in adults is most unlikely, for the latter have no valvular defects, while the former all appear to die at a very early age. It is still possible that cases of infantile fibroelastosis may develop into the adult group, but at the moment the gap in age between the two is formidable. An explanation which seems more acceptable is that both are caused by a similar and as yet unknown mechanism.

Summary

Three cases of fibroelastosis accompanied by aortic stenosis or atresia are described.

Study of these cases and of other published reports shows that fibroelastosis in the first year of life may be divided clearly into two groups for which the terms foetal and infantile fibroelastosis are suggested. The first, manifest at birth, is characterized by early death, aortic stenosis, left ventricular hypoplasia, and right ventricular hypertrophy. The second, usually not

covered until 3 months of age or more, has no valvular defects and shows very considerable increase in heart weight due to gross left ventricular hypertrophy.

On morphological grounds anoxia of the cardiac muscle during cardiac development seems to offer the most acceptable explanation of the changes found at post-mortem examination in foetal and infantile fibroelastosis, and a possible mechanism for this is offered.

The connexion between foetal and infantile fibroelastosis and the endocardial sclerosis found in adults is discussed.

I should like to thank Dr. W. A. Bourne for his advice and encouragement during the preparation of this paper. I wish to thank also Miss M. K. Lawlor and Dr. J. F. Enright for permission to report on patients admitted under their care. Mr. Jackson very kindly photographed the specimens.

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"There is at present a sickness in our country—a sickness of rumour and anxiety, of suspicion and distrust, and, at its worst, of fear and tragedy," said Dr. WEAVER, President of the American Association for the Advancement of Science, in his introductory remarks to the address of the retiring president (*Science*, February 18, 1955). Analysing the causes of this sickness, Dr. Weaver blamed the lack of "constructive courage with respect to the future," the strange lack of faith in scholarly competence, and the misguided zeal of sincere persons with mistaken ideas of good citizenship. At its worst the disease was "the result of political pressure, of personal selfishness, and of the pathological demagogs with small and nasty minds." The effect of these general and recurring fears was that confidence in government promises and even in the "Anglo-Saxon tradition of due process" had been destroyed. Commenting on the universality of this sickness, Dr. Weaver pointed out that science voiced its concern at it, not to demand protection for itself, but primarily because the problem was a universal one. As a remedy he called for the abandonment of timidity, and in its place a "really sensible, constructive stand," giving the warning that wit and patience must be used because "freedom is too precious to deserve rash or stupid support." He hoped that government concern "to improve the whole loyalty-security-secrecy setup" was a sign that the sickness of his country was waning, and at that actual meeting they were celebrating a "rededication to liberal decency."

SOME EFFECTS OF HIGH-ALTITUDE CLIMBING

INVESTIGATIONS MADE ON CLIMBERS OF THE BRITISH KANGCHENJUNGA RECONNAISSANCE EXPEDITION, 1954

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During the 1954 British Kangchenjunga Reconnaissance Expedition the opportunity was taken of carrying out certain biochemical and microscopical analyses of blood and urine samples obtained by the expedition medical officer (D. S. M.) from climbers at various altitudes. These were sent by runners to Darjeeling and dispatched, by aeroplane to the Medical College, Calcutta, for assessment. Although many expeditions to the Himalayas have been made, there has unfortunately been little scientific liaison between them. We understand that samples of blood were collected from climbers of the successful 1953 Everest Expedition and sent back to England for analysis. We have not seen the results of those analyses or of any investigations that may have been conducted by other parties. Referable literature is difficult to obtain.

General Observations

A significant feature worth noting in relation to this expedition was the fact that it was primarily a reconnaissance. Knowing this, the party would be less likely to experience the anxiety stresses that are often associated with the anticipation of future efforts required in attempting to reach the summit. It is usually only at levels above those reached on this expedition that the almost inevitable deterioration occurs, no matter what degree of acclimatization is simultaneously taking place.

Our approach to Kangchenjunga was along the Singalila ridge—a high-level route throughout—which, although relatively arduous, must have been responsible for the high degree of acclimatization attained by all members of the party when base camp 18,000 ft. (5,500 m.) was reached on the eighteenth day out. No climber suffered from headache, nausea, or undue breathlessness except that three members experienced occasional spells of characteristic rapid periodic breathing. Sore throat and gastro-enteritis were rare, and there were no cases of frost-bite. Some of the porters who did not wear sunglasses complained of photophobia, and a mild conjunctivitis was found on examination. It was a revelation to watch some of the porters, barefooted, carry loads through snow and ice, and sleep at night in the open with scanty clothing—such is their ability to acclimatize to cold. The sherpanis—we had 16 of these female porters—performed their duties as well as most of the men.

Rothera tests were performed on numerous occasions on the mountain, particularly after climbers had made

exhausting ascents. On only one occasion was acetonuria found to be present, and that was on the third day out from Darjeeling at 11,000 ft. (3,350 m.). Of the two climbers who had a trace of acetone in their urine, one had enteritis. However, some morning urine samples taken on the mountain and sent to Calcutta contained acetone as detected by the Rothera test. We are at a loss to explain the disparity between the results of tests performed on the mountain and those in Calcutta, unless it is that the mountain tests were performed on samples collected in the evening and those tested in Calcutta were morning urine specimens.

Despite efforts to encourage all climbers to drink large quantities of fluid, the specific gravity of urine specimens obtained from climbers after a day of exertion frequently ranged between 1030 and 1040. It proved impracticable to estimate the total urine output in any one day, but it was apparent that this was reduced. Although members were often dehydrated, thirst, like appetite, tended to be depressed.

The liability to shock following even minor injuries incurred while climbing at high altitudes is noteworthy. It would seem to be somewhat comparable to the increased liability to shock of a woman after a lengthy confinement. One of us suffered a lacerated finger with avulsion of the extensor tendon from the distal phalanx as a result of a blow from falling rock. The degree of shock was out of all proportion to the severity of the injury. Another climber received a lacerated scalp injury from a falling rock. Although the initial shock was minimal, some delayed reaction occurred later. He was confined to bed for 48 hours and forbidden climbing for the remaining week of the trip. Chlortetracycline (aureomycin) was administered on one occasion, but so severe were the toxic effects that the drug had to be stopped. Many of these effects, such as headache, nausea, and vomiting, are aggravated by anoxia.

The following changes in behaviour and thought were noted at the higher altitudes. Memory and concentration were impaired. For example, attempts to memorize from the *Oxford Dictionary of Quotations* failed. When using the cinematograph camera the operator would often forget to turn back the turret after rewinding. Only a routine automatic action can be reliably performed. One periodically became aware of a feeling of mental lethargy, with the result that there was a tendency not to push things to a satisfactory conclusion in the face of difficulties, even though one's physical prowess might not have been exhausted. At meetings held to discuss plans, thinking was not always incisive and conclusive. Insomnia was common; discordant restless mental activity often continued far into the night. Dream content was vivid, as though one had a high fever. There were frequent requests for sleeping pills. It is probable that the effects of altitude were responsible for some unruly behaviour on the part of the porters. Discipline was not always easy to maintain.

Laboratory Investigations

We were hindered by unforeseen difficulties in our attempt to carry out prearranged investigations. The samples were flown to Calcutta from Darjeeling, but there was much unavoidable delay in getting the specimens down to Darjeeling, with the result that many of the blood samples were found to be haemolysed or decomposed when they arrived at the laboratory. The effect of heat would also be responsible for this deterioration. At that time the Calcutta area was in the grip of a heat wave, when the maximum temperature in the shade reached 110° F. (43.3° C.). It is significant that the blood samples taken in Darjeeling and examined in Calcutta during this unusually hot weather were unsuitable, whereas many of those taken later on the mountain were satisfactory. In some cases the blood had completely leaked out of the containers, although they appeared to be leak-proof in the laboratory before packing. Care was taken on the mountain to ensure that the screw caps were tightened. The reduced atmospheric pressure at high altitude might be responsible for this leakage. We could not, therefore, obtain as many samples from various altitudes as we had hoped. On blood samples, haemoglobin percentages were estimated from iron analyses, a method which is considered by King and his associates (1947, 1948a, 1948b) to be the most reliable, although, of course, it is not absolutely free from error, because a certain small proportion of the iron, from 0.1 to 0.3 mg., is present per 100 ml. of cell-free plasma. Estimations of sodium, potassium, adrenaline, and sugar could not be done. For the study of white cells we had to be satisfied with a differential leucocyte count taken from thin films made on the mountain and sent down to the laboratory. Urine samples were tested for acetone, and quantitative analysis of chlorides was performed.

Haemoglobin Content of Blood.—Samples of blood from six climbers collected at 17,000 ft. (5,200 m.) and from four climbers collected at 21,000 ft. (6,400 m.) were available for examination. Of those collected at 17,000 ft. the iron content ranged from 52.6 to 95 mg. per 100 ml. of blood, with a mean of 74.1 mg. per 100 ml. Translated into grammes of haemoglobin per 100 ml., this comes to 15.7 to 28.4 g. per 100 ml., with a mean of 22.18 g., the percentage of iron content in haemoglobin being 0.334% (Hupfner). Of the samples collected at 21,000 ft. the iron content ranged from 57 to 64.5 mg. per 100 ml., with a mean of 61.6 mg. (17 to 19.3 g. of haemoglobin per 100 ml., with a mean of 18.4 g.).

Chloride Content of Blood.—Estimation of chloride on the above-mentioned blood samples showed a range from 419 to 620 mg. per 100 ml., with a mean of 509 mg.

Leucocyte Picture.—Films from four climbers collected at 17,000 ft. (5,200 m.) and from one collected at 21,000 ft. (6,400 m.) were available for examination. A study of the stained thin films did not suggest any lymphocytopenia or any significant eosinopenia; nor was there any suggestion of a qualitative change in the lymphocytes as found by Frank and Dougherty (1953) in their experimental studies on the effects of stress.

Acetone Bodies in Urine.—Of the two samples of urine collected from two climbers at Darjeeling, neither showed the presence of acetone bodies. Of the six samples collected from six climbers at an altitude of 17,000 ft. (5,200 m.), two gave definite reaction for acetone bodies, one gave a doubtful reaction, while the remaining three gave negative reactions. Of the two samples collected at 21,000 ft. (6,400 m.) from two climbers, both gave a definite reaction for acetone bodies.

Urinary Chloride and Creatinine.—Two samples of urine from 6,700 ft. (2,040 m.), six from 17,000 ft. (5,200 m.), and two from 21,000 ft. (6,400 m.) were available for examination. The mean chloride contents were 1.34 g., 0.878 g., and 0.7 g. per 100 ml. respectively, and the mean creatinine contents were 0.108 g., 0.128 g., and 0.169 g. per 100 ml. respectively.

Summary

A study of the climbers taking part in the 1954 British Kangchenjunga Reconnaissance Expedition was made in an attempt to assess some of the physiological changes which occur at high altitudes. Some general clinical observations are made on the stresses which occur. The results of a small number of blood and urine analyses are recorded.

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DERMATOMYOSITIS

A CASE REPORT WITH POST-MORTEM FINDINGS

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Dermatomyositis is an unusual condition in which pathological changes occur not only in the skin and muscles but also in other organs. Such changes have often been reported, and Wainger and Lever (1949), in their study of three cases with post-mortem findings, concentrated their attention on those changes in tissues other than muscle and skin. They were unable to report any specific renal changes either in their own cases or in those from the literature. The fact that renal lesions, hitherto undescribed, have been found in the present case is considered sufficient justification for putting it on record. The unusual severity, the presence of jaundice, and the response to cortisone are further interesting features.

Case Report

A male office-worker aged 30, whose past medical history revealed only pleurisy with effusion in 1947, said that his present illness had started with a severe sore throat about ten days before admission to hospital on April 6, 1954. He was confined to bed, without any specific treatment, for three days. He got up on the fourth day, but because of headache, shivering, and a feeling of nausea, did not feel very well. There was no vomiting. Three days before admission he had a good deal of pain in both ankles and marked sweating. In the 24 hours preceding admission both his ankles became swollen and he had pain in his right knee- and wrist-joints. There had been no upset of bowels or micturition, but appetite had been poor for the previous fortnight.

Examination revealed a thin man, very flushed and sweating profusely. His temperature was 102° F. (38.9° C.). There was marked swelling of the left ankle- and right knee-joints. The skin over the joints was flushed, but not more so than the skin in other areas. These swellings were tender and joint movements were limited. There was some tenderness and limitation of movement in the right elbow- and wrist-joints but no visible swelling in these areas. Muscle tenderness was present, especially in the left calf, but the chief finding was of pain on joint movement. His pulse rate was 120 and B.P. 120/70; there were no murmurs. No abnormalities were observed in other systems and tendon responses were normal. A provisional diagnosis of acute rheumatic fever was made and the patient was started on salicylate therapy.

About 12 hours after admission his condition did not seem to be satisfactory. His pulse rate was increased to 130, and he was restless and complained of a good deal of pain in the right forearm. B.P. 100/70. Examination of the right forearm revealed a turgid, brawny swelling of the muscles, which showed the characteristics of a cellulitis. Joint movement was limited, and there was marked muscle tenderness. One was somewhat surprised to find a swelling of such dimensions that had not been present at the time of admission. A white blood count revealed a leucocytosis of 22,000 per c.mm. (96% polymorphs, 4% lymphocytes); Hb, 106%; E.S.R. (Wintrobe), 33 mm. in one hour. The urine contained a trace of albumin and there was a very heavy deposit of creatine. This latter finding, together with skin and muscle involvement, suggested the diagnosis of dermatomyositis.

The following day cortisone, 50 mg. twice daily by mouth, was given. During the next three days the patient's condition varied considerably. An improvement was noted by the gradual return of the pulse rate towards normal and the lessening of joint and muscle pain. Further swellings occurred, however: his right wrist- and left elbow-joints and the muscles of the right calf became, in turn, swollen and tender. There was no swelling of trunk muscles, and the orbital tissues were not involved. These swellings occurred with amazing rapidity and seemed to reach a maximum in about six to eight hours and slowly resolve over a period of several days. About the fourth day a diffuse, erythematous mottling was noted in the swollen areas, and later this extended to the trunk and limbs but avoided the face. The dosage of cortisone had to be reduced to 75 mg. daily to prevent hypertension.

On the third day the patient felt nauseated, and vomited several times. Later he developed hiccup. The abdomen was distended and bowel sounds were few. Blood urea amounted to 177 mg./100 ml. Intravenous fluids were given and a Ryle tube was passed with intermittent gastric aspiration. The next day he was jaundiced and the urine contained bile pigments. The serum bilirubin test, performed on the fifth day, was 8.25 mg./100 ml. Although jaundice and paralytic ileus was present, the disease process seems to have been contained, for the skin and muscle swellings became less, and on the sixth day, although the patient was critically ill, there was no dermatomyositis.

On the evening of the sixth day bowel sounds were returning and flatus was passed. Blood urea was now 223 mg./100 ml. The E.C.G. was within normal limits and there was no electrolye imbalance. The following day he was definitely deteriorating and at times irrational. His mouth was dry and the tongue glazed and swollen. He became comatose and died in the evening of the seventh day after admission.

Pathological Findings

The post-mortem examination was performed 12 hours after death. The subject was a thin male, moderately jaundiced. There was no evidence of swelling in muscles or skin, but well-marked desquamation was present on the arms and hands. Almost all the abdominal viscera were enlarged and flabby. There was some congestion of the mucous membrane of the stomach but no gastric or enteric ulceration.

The skin showed moderate keratinization but no general epidermal thickening. In the rete area there was a moderate round-cell infiltration. In the dermis the fibrous tissue bundles were loosely arranged and broken up. The deeper fat was rather increased and the sweat-gland epithelium showed infiltration with fatty droplets.

Heart Muscle.—Myocardium flabby. Weight 400 g. The cardiac muscle fibres showed fragmentation, with variation in size and shape. The nuclei remained normal on the whole. No changes in the larger or smaller vessels were seen.

Voluntary Muscle.—Many of the fibres had disappeared, but the structure remained normal so long as any portions remained. Striation was well marked. Many sarcolemmal nuclei were seen left free between the remaining fibres, and in places proliferative overgrowth of these nuclei was seen. Groups of pigment granules, negatively staining for iron but positive for melanin, were apparent here and there within sarcolemma sheaths or between fibres.

Adrenals.—Marked oedema, with cortical capillary haemorrhages and disappearance of many cells. Other cells showed loss of nuclei and irregular staining of remaining cytoplasm.

Lung.—Oedema only. Generalized capillary congestion with small haemorrhages. Oedema, patchy in distribution. In places there was endothelial proliferation of the alveolar lining. There was some thickening of peripheral fibrous coat in the arterioles. The interstitial tissue contained plasma cells with focal distribution. A moderate number of pigment-containing macrophages were also present.

Kidneys.—Both flabby, with yellow fatty streaks. 300 g. each. *Cortex:* Some glomeruli were congested: others showed hydropic degeneration. The convoluted tubules showed a marked degree of degenerative change, ranging

from cloudy swelling to necrosis. *Medulla:* A similar degeneration of the straight tubules, many of which contained blood casts. The vessels showed some thickening, chiefly of the muscle coats.

Liver.—2,000 g. Flabby, yellow, and fatty. The cells were irregular in size and shape and were separated by spaces. No cirrhosis or congestion was seen. In the portal areas the vessels and ducts appeared thickened, with loose fibrous tissue rather irregularly disposed. Some lymphocytic infiltration was also present in these areas.

Pathological Data

Date	Throat Swab	Urine	Blood Urea	Serum Creatine	Serum Creatinine	Serum Bilirubin
6/4/54	Predominant growth *Str. viridans*	Acid. Creatine + +. Many white and red cells. No casts				
9/4/54		Creatine, 840 mg./24 hrs. Creatinine, 1,100 mg./24 hrs.	177 mg./100 ml.	8 mg./100 ml.	4·5 mg./100 ml.	
12/4/54			215 mg./100 ml.			8·25 mg./100 ml.

Discussion

Not only was this case particularly acute and severe but it also presented the unusual features of kidney and liver involvement. It is extremely difficult to evaluate the significance of these hepatic and renal changes. To say that the patient died from a hepato-renal syndrome although the polymyositis was contained is not really informative, neither is it fully in accordance with the facts. The term "hepato-renal syndrome," however poorly defined, would appear to include patients dying often in coma, usually jaundiced, and in whom renal and hepatic damage is demonstrated microscopically. In the kidney severe tubule necrosis, most marked in the convoluted tubules, and in the liver cellular damage, which appears to be further enhanced by the presence of excess bile which stains the liver cells, are the usual histological findings (Dible, 1953). In the case under discussion there was very marked renal damage amounting to a cortical necrosis. Microscopically there were changes in both cortex and medulla. The glomeruli were congested, while the convoluted tubules showed a wide range of degenerative change. The liver cells were not bile-stained and there was no evidence of a primary causative lesion. There seems, then, to be considerable evidence to support the view that the renal lesions in this case resulted from the disease process of dermatomyositis.

It is interesting to record the similarity between the nature of renal lesions occurring in other collagen disease, such as disseminated lupus erythematosus and polyarteritis nodosa, and that of the renal lesions here described. In the two former conditions it is a well-established fact that cortisone and A.C.T.H. may suppress all evidence of the disease except when renal lesions occur, in which case the processes are invariably progressive. A similar failure of these hormones would appear to have been responsible for the advanced renal disease in this case. Ragan (1950) reports improvement in two long-standing cases of dermatomyositis treated with A.C.T.H. In the most recent case report by Clein (1953) mention is made of the benefit derived from cortisone and A.C.T.H. He used both hormones with equal success. He also stressed the high polymorphonuclear leucocyte count, which was also present in the case under discussion.

Summary

A case of acute dermatomyositis with necropsy findings is reported. Renal lesions thought to have resulted from the disease process are described. These do not seem to have been recorded previously. The response of the muscle and skin lesions to cortisone is noted, while the hormone appears not to have influenced the kidney damage.

It is a pleasure to acknowledge the help and advice of Dr. A. Nelson-Jones, under whose care the patient was admitted. Dr. E. James also gave much helpful advice. Dr. S. Marshall kindly supplied the detailed histological report and Dr. F. Brafield did the biochemical investigations. Miss H. Child was most helpful with the clerical work.

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Medical Memoranda

Tropical Pulmonary Eosinophilia in a West African

This paper reports a case of tropical pulmonary eosinophilia in a Nigerian. So far as can be determined, this condition has not been previously reported as occurring in a West African.

Case Report

The patient was a male Nigerian aged 45, whose occupation was a leprosy inspector.

Previous History.—In 1943 he had pneumonia affecting the left side of the chest and was in hospital for three weeks, being treated with sulphonamides. He was in the Army, in Burma, from 1944 to 1946, and in 1944 had pneumonia affecting both sides of the chest. He was ill for five weeks and was treated with penicillin and sulphonamides. In 1946 he was given oil of chenopodium for ascariasis. Later that year he was discharged from the Army in the Owerri province of Nigeria. He remained there until 1952, when he went to Calabar. He returned to Owerri province one month before he was seen with the current complaint.

Present History.—For six weeks he had complained of swellings in the skin on different parts of the body, each lasting a few days. Three weeks before being seen he had developed a dry cough, which was worse on lying down. The cough had improved slightly during the last week. For three weeks he had been short of breath on exertion—for example, on riding his bicycle on the flat. He also complained of a burning sensation all over the inside of his chest, and had been feeling generally off colour.

Examination showed that he was well nourished. Swellings were seen on right cheek, right calf, and right forearm which were probably Calabar swellings. Respiratory system: no impaired movement of the thoracic cage or impaired percussion note; medium crepitations present at both lung bases. Cardiovascular system: N.A.D. Gastro-intestinal system: N.A.D. No hepatomegaly or splenomegaly. Other signs: lymph nodes in the groins and axillae were palpable but unlikely to be pathological. The patient was apyrexial.

Laboratory Investigations.—Haemoglobin, 14 g.%; R.B.C., 5,380,000 per c.mm.; W.B.C., 37,800 per c.mm. (polymorphonuclear leucocytes 5%, eosinophils 88%, lymphocytes 7%). No microfilariae were seen in thick blood films made at 12 noon. No autohaemagglutination occurred either at room temperature or when the blood was put into a refrigerator. The stool did not contain any helminth ova. Sputum: no specimen available. *X*-ray not available.

The blood count remained of the same order over the next seven days, after which penicillin therapy was started with 300,000 units daily for three days Unfortunately the patient did not receive a full course of penicillin, as the observer left Nigeria at that point. One week after the beginning of the penicillin therapy the total white cell count

had fallen from 37,800 to 24,700 per c.mm. and the eosinophils from 88 to 73%—that is, from 33,264 to 18,031 per c.mm. Two months later, without any further treatment, the white cell count had fallen to 9,400 per c.mm. and the eosinophils to 60% (5,640 per c.mm.). Four months after penicillin the white-cell count was 12,000 per c.mm. and the eosinophils 57% (6,840 per c.mm.). The patient stated that he felt better.

COMMENT

It is regretted that an *x*-ray examination of the chest could not be undertaken. However, in view of the clinical and haematological findings it would appear likely that the patient was suffering from tropical pulmonary eosinophilia. The possible presence of a *Loa loa* infection would produce a degree of eosinophilia, but hardly one of 88% (33,264 eosinophils per c.mm.). There was no evidence to suggest the presence of another helminth infection. Hunter (1946) reported a case of tropical pulmonary eosinophilia in a European aged 37 who had been resident in Nigeria for 12 years. Wilson (1947) reported the condition in three Africans in East Africa, but it is believed that the present paper reports the occurrence of the condition in a West African for the first time. It is interesting to speculate whether this patient acquired the disease in India some eight years previously and that it had only become manifest recently, or whether it had been acquired in Nigeria.

It is not possible to say with any assurance whether or not there had been any response to penicillin in this case, although there is a suggestion that the drug had some effect.

This case was seen at the Leprosy Research Unit, Uzuakoli, Nigeria. Thanks are due to Dr. J. Lowe for permission to investigate the case and to publish the findings, and to Sister O. Smith for her co-operation.

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Long-term Prognosis in Infantile Eczema

In 1953 Purdy published the results of an investigation into the after-history of cases of infantile eczema in Edinburgh. To amplify his findings a similar investigation into the cases of infantile eczema occurring in Dundee over the same period was carried out. Letters were sent to those patients who attended the skin department of Dundee Royal Infirmary with infantile eczema during 1931–7 inclusive. The questionary adopted was the same as that used by Purdy, but in addition questions were included regarding the onset and disappearance of asthma. In order to have results as closely related as possible to those of Purdy, the same criteria were followed in the selection of cases from the hospital records.

RESULTS

In a large number of cases it was impossible to locate by letter persons whose last known address was that of 15 to 22 years ago. Thus Table I shows that, of 136 questionaries sent out, 92 (67.6%) were returned as "dead" letters.

TABLE I.—*Result of Questioning*

Total No. of persons sent letters	136	(94 males, 42 females)
"Dead" letters returned	92	
Useful replies	37	(20 males, 17 females)
Useless replies (deaths at early age)	2	
Replies not returned	5	

In the 37 useful replies received, 12 patients claimed to have had no sequelae to their primary attack of infantile eczema. Table II gives the incidence of the generally accepted sequelae and compares the figures found in this study with those in Purdy's series. In assessing the final results of the Besnier's prurigo group all patients were examined personally unless they had been seen recently by a consultant of this department.

TABLE II.—*Results of 37 Replies*

	No.	Asthma	Asthma Denied; Wheezing Admitted	Hay-fever	Besnier's Prurigo	Migraine
Male	20	9	1	5	10	1
Female	17	4	4	5	5	3
Total	37	13 (35·1%)	5 (13·5%)	10 (27%)	15 (40·5%)	4 (10·8%)
Purdy's series	93	37 (39·8%)	10 (10·7%)	39 (41·9%)	23 (24·7%)	7 (7·5%)

The overall figure for asthma is 35.1%. If the five patients who failed to return the questionary are classed as having no asthma then a minimum figure of 30.9% is reached. This minimum is too low, as it assumes that none of the wheezing group of five patients and none of the "lost" five patients are asthmatic. If it is conceded that the wheezing group are asthmatic a minimum of 42.8% is reached, and excluding the "lost" five patients the figure is 48.6%. This range of roughly 43 to 49% is similar to Purdy's of 30 to 50%. Asthma developed in 13 patients in the first decade and disappeared in four males and one female in the second decade.

The figures for Besnier's prurigo show a range of 35.7 to 40.5%; the minimum figure presumes a complete absence of the complaint in the five patients who failed to return the questionary.

Table III shows a regrouping of the patients and agrees with Purdy that asthma without skin involvement is the most frequent sequela, with a range of 23.8 to 27%.

TABLE III.—*Regrouping of Cases from Table II*

	No.	Asthma (or Wheezing Attacks) but No Besnier's Prurigo	Besnier's Prurigo but No Asthma (or Wheezing)	Both Asthma (or Wheezing) and Besnier's Prurigo	Hay-fever but No Asthma (or Wheezing)
Male	20	5	5	5	1
Female	17	5	2	3	
Total	37	10 (27%)	7 (18·9%)	8 (21·6%)	1 (2·7%)
Purdy's series	93	27 (29%)	5 (5·4%)	20 (21·5%)	14 (15%)

Besnier's prurigo in association with asthma is next in frequency, with a range of 19 to 21.6%. Besnier's prurigo alone has a range of 16.6 to 18.9%, which is much higher than that observed in Purdy's series—namely, 4 to 5.4%.

Hay-fever was present in 27% cases in Table II, but in the regrouping in Table III only 2.7% claim to have hay-fever without asthma.

Migraine occurred in four patients, three of them females. I agree with Purdy that it is a very doubtful outcome of infantile eczema.

The answers to questions regarding nervous stability and intelligence were so varied that it was impossible to support or refute the widely held belief that sufferers from infantile eczema are compensated with a high intelligence.

COMMENT

Of the 37 (27%) useful replies received to a questionary similar to Purdy's, 25 describe at least one of the recognized sequelae of infantile eczema. Of these 25, 10 had asthma, 8 Besnier's prurigo and asthma, and 7 Besnier's prurigo alone. Although the number of useful replies in this investigation was disappointingly low, it was decided to publish the results so that they may be added to Purdy's findings, and to any subsequent figures recorded from other centres, in order that the ultimate total number may be high enough to yield an accurate picture of the sequelae of infantile eczema.

I wish to thank Dr. J. Kinnear for permission to use his cases and for his helpful advice.

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Reviews

ALMROTH WRIGHT

Almroth Wright—Provocative Doctor and Thinker. By Leonard Colebrook, F.R.S. (Pp. 286; illustrated. 21s.) London: William Heinemann Medical Books Ltd. 1954.

The story of Almroth Wright is told sharply and succinctly by Leonard Colebrook in his foreword—how he worked in the laboratory away into the night; how when he met with difficulties he developed new techniques to overcome them; how he turned his laboratory at St. Mary's into a vaccine therapy clinic; how he charmed the patients and young men whom he attracted to work with him for a pittance; and how throughout a larger part of his life his spare time was spent in writing a treatise on morals, a treatise which had not appeared when he died in 1947.

There is no doubt that Wright was a great man, and there is no doubt also that he was appreciated abroad more than at home. I saw that when I accompanied him to France in October of 1914. He was a consulting physician in the Army Medical Service, and when he visited French laboratories he was worshipped almost as much as Pasteur.

His great work was vaccine therapy, beginning with anti-typhoid vaccine and spreading to a great variety of infections, but, as the author of this book points out, he did many other good things. Indirectly his work on immunization was the means of bringing the bacteriologist into contact with the patient, thus changing his status from a servant of the clinician to a colleague who was called into consultation like any other "consultant." For this the laboratory workers of the present day should offer him thanks. The author traces his career from the beginning, but naturally by far the greater part of the book is devoted to his work after he left the Army Medical College and came to St. Mary's. There Colebrook was one of his early assistants and his disciple. He tells of the work done in what were quite inadequate laboratories with hardly any equipment except glass tubing, a blow-pipe, and some rubber teats. But out of that work came vaccine therapy.

Then there was his work on septic wounds done in the Casino at Boulogne in the first world war; his serious controversies with Watson Cheyne and others; and his later years somewhat tinged with loneliness.

Colebrook was, of all Wright's pupils, the one who saw most of his private life, and he manages to give a picture of the scientist and the man which is very fascinating. It is of especial interest to me as one who worked in Wright's laboratory from 1906 till he died, but no one who likes to read of great men could fail to enjoy the book and profit by it.

ALEXANDER FLEMING.

⁂ This review was written shortly before Sir Alexander Fleming's death.—ED., *B.M.J.*

HISTORY OF COMMON DISEASES

The History and Conquest of Common Diseases. Edited by Walter R. Bett, M.R.C.S., L.R.C.P. (Pp. 334. $4.) Norman: University of Oklahoma Press. 1954.

This is a book which the "physician of two continents" would have approved, not only as a medical historian, but because it is an example of the collaboration between British and American doctors which he did so much to encourage in his lifetime. Dr. Bett, through his associations with the United States, is thus promoting Anglo-American friendship in the true spirit of William Osler.

This book, which replaces *A Short History of Some Common Diseases*, edited by Dr. Bett in 1934, is "mainly for patients, but also for the medical profession." Six of the contributors to this volume belong to the United States. Dr. George Rosen, of Columbia University, writes on acute communicable diseases. His history of diphtheria is excellent. The waxing and waning of this disease is remarkable and might have been further emphasized. When it reappeared about the middle of the nineteenth century, at Ash in Kent, it was then so rare that it was unrecognized by most practitioners, and Simon sent Greenhow and Burdon-Sanderson to investigate outbreaks where it was prevalent. Dr. L. J. Moorman, of Oklahoma City, contributes a history of tuberculosis, but does not allude to the great impetus that was given in this country to medical research and treatment of the disease after 1912. Bodington, incidentally, spelt his name with one *d*. Dr. E. F. Hartung, of New York University, writes on arthritis. An admirable account of the history of Bright's disease is given by Dr. R. H. Major, of the University of Kansas; Dr. D. C. Balfour, Chief, Surgery Division, Mayo Foundation, writes on gallstones; and Dr. W. G. Lennox, of Boston, lucidly traces how the belief that epilepsy was a demoniac possession came to be replaced by modern scientific knowledge.

Of the British contributions one would single out as specially interesting—Dr. Terence East on heart disease, Dr. W. S. C. Copeman on rheumatism, Dr. A. W. Cawadias on diseases of the endocrine glands, and Dr. Bett on appendicitis. The chapter on pneumonia by Dr. E. M. Brockbank and Dr. W. Brockbank reveals how strikingly sulphonamides and penicillin have altered the clinical picture of this disease. Dr. A. White Franklin sketches the history of rickets from Galen to Mellanby, giving due meed of recognition to Daniel Whistler, whose M.D. thesis on rickets at Leyden in 1645 preceded Francis Glisson's famous book of 1650–1. Dr. E. L. Murphy's account of malingering is of value, and Chapter 16, by Mr. Harold Burrows, gives in succinct form an excellent account of the development of knowledge of cancer. The bibliographies are full and useful.

Dr. Bett and his contributors are to be congratulated, while a word of praise is due to the University of Oklahoma Press for the presentation of the volume.

ARTHUR S. MACNALTY.

BIOPHYSICS AND BIOPHYSICAL CHEMISTRY

Progress in Biophysics and Biophysical Chemistry. Volume 4. Edited by J. A. V. Butler and J. T. Randall, F.R.S. (Pp. 339 + viii; illustrated. 63s.) London: Pergamon Press. 1954.

The volume under review provides a refreshing change from some of its predecessors; not only have the editors chosen their subjects wisely, but also—and this is more important perhaps—they have chosen as authors workers who are competent to write in their respective fields.

The problems associated with muscular contraction are dealt with in two articles—"The Transference of the Muscle Energy in the Contraction Cycle," by Weber and Portzehl, and "Facts and Theories About Muscle," by Wilkie—while the behaviour of polyelectrolyte gels, which must be understood if the more physical aspects of muscular contraction are to be elucidated, has been described by Katchalsky. Fernandez-Morán has given a good account of the increase in our knowledge of the structure of the nerve fibre provided by polarization optics, *x*-ray diffraction studies, and the electron microscope; to a physiologist perhaps the most striking feature of the work is the excellent accord between the calculations of the *x*-ray diffractionist and the observations of the electron-microscopist. The *x*-ray diffraction picture of a nerve is a series of spots on a photographic plate; by what must seem to the uninitiated a supernatural intuition the physicist can, from the shapes, positions, and blackness of the spots, state that the myelin sheath is made up of concentric shells some 180 A thick; under the electron microscope the shells can actually be made visible and measured.

The cause of cancer is most probably to be sought in the pathology of the cell nucleus; it will therefore be satisfying to those who seek some justification for pure research to see in two articles—"The Nucleoprotein Complex of the Cell Nucleus and its Reactions," by Davison, Conway, and Butler, and "Chromosome Breakage," by Koeller—how modern physical and physicochemical techniques are revealing more and more of the secrets of this all-important body. Finally, the present volume contains an article by J. C. Kendrew, "The Crystalline Proteins: Recent *X*-ray Studies

and Structural Hypotheses." This is necessarily abstruse for the biologist, and its main value here resides in the candour of the author, who modestly emphasizes the paucity of definite knowledge in this field. The most spectacular advances in our knowledge of protein structure have resulted from studies on the fibrous proteins like keratin; such advances have contributed to our knowledge of the physiology of muscle and nerve. The crystalline proteins, such as insulin, albumin, and globulin, present far more serious problems in methodology, but their solution is a pressing need if we are to relate, for example, the phenomena of immunochemistry with the morphology of the proteins that are concerned.

H. DAVSON.

THE OSTEOCHONDROSES

Legg–Calvé–Perthes Syndrome and Related Osteochondroses of Youth. By Charles Weer Goff, M.D., in association with Ned M. Shutkin, M.D., and Myerma R. Hersey, M.S. (Pp. 332+xxiii; illustrated. 77s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954.

This book contains all the important known facts and theories of osteochondritis deformans juvenilis and the related lesions of other epiphyses. The name of pseudocoxalgia is discarded and the group named osteochondroses is defined. The author, who had the assistance of Jacques Calvé before his death (he wrote the foreword), has extracted material from the enormous quantity of literature that has been accumulating for 45 years and made observations on groups of children.

This study of a condition which so often causes permanent damage to an epiphysis is most thorough; the subject is well presented and the excellent radiographs are most fascinating. It is a specialist book, and the reader will seek for the cause of the changes in the epiphysis. The "Murk Jansen and Perkins discussion" is reported (Jansen's photograph, but not that of his opponent, is reproduced). Almost all the special examinations and observations were found to be negative, and so did not prove helpful in elucidating the aetiology. However, it is stated that the "constitutional preterminators are proven factors of causality," and environmental factors, such as trauma, are superimposed. Remissions with a second centre developing in the epiphysis are stated to be more common than is usually supposed. Modified recumbency treatment is recommended. An important observation is that every patient who had been followed up for ten years or more, and who was 20 years of age or older, had symptoms of dysfunction. The reports on related osteochondroses follow a similar pattern and are well collected.

An appendix forms a charming tribute to Mrs. Smith, of Farmington, Connecticut, who remodelled on the English system a small farmhouse for the accommodation of ten crippled children. Like several in this country it has grown, and now has nearly 200 beds.

There are a bibliography, an author index, and a subject index, and the author explains his system of references. Even so, the reader will not necessarily be able to find what he may require. For instance, use is made of Burrows's classification and 1950 is placed after his name, but there is no mention of the paper in the bibliography.

This book will be of great help to all dealing with bone diseases in adults as well as in children.

ST. J. D. BUXTON.

SKIN HISTOPATHOLOGY

Histopathology of the Skin. By Walter F. Lever, M.D. Second edition. (Pp. 518+xviii; 281 illustrations, 8 in colour. 96s.) London, Philadelphia, Montreal: J. B. Lippincott Company. 1954.

The second edition of this textbook has been considerably modified and added to in certain sections. As before, the author includes a very short clinical note on each disorder, primarily for the benefit of the pathologist, though in many cases this is of somewhat doubtful value. It is difficult, though not impossible, to think of a few uncommon disorders which a careful search fails to reveal in this treatise, but the book would no doubt be used for a very long time in current histological work before these omissions were discovered. It has in the past been largely left to dermatologists to develop the study of skin histopathology, and even now, in many places, the pathologist prefers to leave this branch of histology to the clinical dermatologist.

Dr. Lever's book will help to facilitate very greatly more widespread knowledge of dermal histology. The views expressed are thoroughly up-to-date and carefully considered, though in a work of this size there is little room for full-length discussion. This possible drawback is overcome by a well-chosen bibliography, divided into sections, which appears at the end of each chapter. The illustrations are good and show clearly what they are meant to show. There can be little doubt that this is now the best book of its kind, whether as a work of reference, a textbook, or a practical bench-side handbook. Both dermatologist and pathologist need it.

F. RAY BETTLEY.

THE VITAMINS

The Vitamins: Chemistry, Physiology, Pathology. Volume III. Edited by W. H. Sebrell, jun., and Robert S. Harris. (Pp. 665+xi. $15.) New York: Academic Press, Inc. London: Academic Books Ltd. 1954.

It can be said at once that Volume III of "Sebrell and Harris" lives up to the high standard set by Volumes I and II, reviewed in these columns earlier this year (January 29, p. 272). This instalment completes the work, which, all in all, provides us with the most comprehensive, the most up-to-date, and the best-documented treatment of the biochemistry of the vitamins so far published.

The third volume contains chapters on the following factors: *p*-aminobenzoic acid, pteroylglutamic acid (i.e., the folic acid group), vitamin B_6 (pyridoxin and related compounds), riboflavin, thiamine, vitamin E, and lastly certain new, and as yet unidentified, growth factors. As in earlier volumes, the emphasis is particularly on biochemistry, although physiology and pathology are not overlooked. Clinical aspects and the methods of assay of vitamins are but briefly referred to, as these topics are already dealt with pretty fully in other compendious treatises available elsewhere. Twenty-three authors contribute to the present volume, all but one being American. The exception is Professor B. C. P. Jansen, the doyen of Dutch biochemists, and distinguished as the first to isolate pure crystalline vitamin B_1.

LESLIE J. HARRIS.

LABORATORY TECHNOLOGY

An Introduction to Medical Laboratory Technology. By F. J. Baker, F.I.M.L.T., F.R.M.S., R. E. Silverton, A.I.M.L.T., F.R.M.S., and Eveline D. Luckcock, A.I.M.L.T. (Pp. 330+x; illustrated. 30s.) London: Butterworth and Co. Ltd. 1955.

This modest volume from the technical staff of the Brompton Hospital aims at meeting the needs of student technicians who are preparing for the Intermediate Examination of the Institute of Medical Laboratory Technology. It consists of short descriptions of elementary laboratory methods, including such items as the cleaning of glassware, simple chemical tests, physiological techniques, sterilization methods, and haematological techniques.

There is naturally little to be found here that is not discussed more fully in larger works, but it will no doubt be very convenient for the student technician to find the material all within the covers of one book. As a minor criticism, the directions given are not always sufficiently fool-proof or explicit. For example, on page 283 we are told "the cork borer must be sharp," but the reader is not told what is to be done when it is blunt. Similarly, on page 248 the use of chloroform for killing animals is described without any indication of how it is introduced into the container.

The book is well produced, with a number of useful illustrations, which accounts for the rather high price. On the whole it will prove useful for the purposes intended, and can be confidently recommended to student technicians who feel the need for a special book on their subject.

N. F. MACLAGAN.

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RADIATION HAZARDS OF EXPERIMENTAL NUCLEAR EXPLOSIONS

The radiation injuries received by the crew of the Japanese boat *Fukuryu Maru*, with the subsequent death of one of them, gave the first inkling of the scale of radiation hazards associated with the testing of the latest nuclear weapons. But it was not until the recent official report issued by the U.S. Atomic Energy Commission[1] that the true magnitude of the problem became evident. The report deals mainly with the damage caused by the fall-out—that is, the deposition of radioactivity in the vicinity of the explosion. The amount of radioactivity in a fall-out may be measured in units of roentgen square miles, which is the product of the dose in roentgens which a person would receive, multiplied by the total area over which the fall-out occurred. The Bikini bomb tested a year ago gave a fall-out amounting to 20 million roentgen square miles[2]; since the area covered by the fall-out was about 8,000 square miles, the total dose delivered there, as from one hour after the explosion, was about 2,500 r.

Since the fall-out occurs over a limited area, which in the case of a test would normally be uninhabited, it does not present a very serious problem, except for unfortunate accidents as with the *Fukuryu Maru*. There is, however, the important problem of the radioactivity other than in the fall-out. A bomb with an explosive power one thousand times that of the Hiroshima type may produce, one hour after the explosion, a total amount of radioactivity equal to about 100 million roentgen square miles. Most of the radioactive fragments are sucked up with the hot gases resulting from the explosion and reach great heights, probably over 100,000 ft. (30 km.). Very little is known about the movements of the atmosphere at such heights, but it is likely that the radioactive cloud would circulate the globe many times before all the particles drifted down to the surface. Much comfort has been derived from the fact that during the long time it takes the particles to settle down most of the radioactivity would have died out. But this safety factor has been overrated. If the radioactive dust took six months to settle down instead of six days, the residual dose delivered would be reduced only by one-half. What is more important is how long the fine dust will stay on the surface before it is washed away by rain or removed by other means; this again is difficult to assess.

The calculation of the global dose resulting from one test is dependent on so many unknown factors that at best it would give a rough estimate. There is, however, no need for such calculation, for some informative data are available. The U.S. report states that the total amount of radiation received from all nuclear detonations so far is about 0.1 r. Although this figure refers to residents of the United States, it presumably applies to any other country. In assessing the significance of this dose it may be pointed out first that, although the report attributes it to the considerable number of atomic explosions carried out so far, probably most of the dose came from the very few hydrogen bombs tested about a year ago. This is so because one H-bomb produces from 100 to 1,000 times more radioactivity than an atom bomb; the contribution of the latter may thus be neglected. The natural background of radiation, due to cosmic rays and the radioactive substances normally contained in the atmosphere, amounts to about 0.1 r per year. We may infer, therefore, that a continuation of tests on the 1954 scale—that is, several H-bombs a year—would double the natural amount of radiation.

What is the consequence of such a world-wide increase in radiation? So far as somatic damage is concerned it is quite negligible. The maximum permissible dose established for those occupationally exposed to radiations is 0.3 r per week, or 15 r per year. From the genetic point of view, however, there is no maximum permissible dose, since every increase of radiation is harmful. In setting up the maximum permissible doses account was taken of the fact that only a small fraction of the population, less than 1%, is habitually exposed to radiation. When the whole population is exposed, the dose considered genetically safe must be reduced correspondingly, which brings it down to about 0.1 r per year. It may be argued that the whole population is already subject to exposures in various radiological examinations. In fact the U.S. report states that the dose of 0.1 r is received in a single chest *x*-ray examination. But such a comparison is misleading. For the genetic hazard only the dose delivered to the gonads is of significance,

[1] *The Effects of High-Yield Nuclear Explosions*, U.S., A.E.C., February, 1955.
[2] Lapp, R. E., *Bull. Atomic Scientists*, 1955, **11**, 45.
[3] *Brit. J. Radiol.*, 1952, **25**, 387.

and furthermore it has to be averaged over the whole population. A survey[3] carried out several years ago in Great Britain has shown that the mean gonad dose received during chest radiography is about 0.0007 r. Even taking into account the much bigger doses received during examination of the pelvis, the survey shows that the mean dose per head of the population from all *x*-ray diagnostic examinations is 0.005 r per year, or one-twentieth of the natural radiation level.

It is very difficult to estimate the genetic damage which may be caused by raising the level of radiation by 0.1 r per year. Most of the evidence about the rate of radiation-induced mutations comes from experiments on *Drosophila*; only in recent years have experiments been made with mice, but these are not yet complete. At the moment the most probable figure for the dose necessary to double the rate of mutations is 30 r per generation. For man this would correspond to a dose rate of 1 r per year. A dose rate of 0.1 r per year would therefore cause a 10% increase in the rate of mutation, which is by no means negligible. But the assumption that the doubling dose is the same in man as in *Drosophila* is not well founded. Some genes are known to undergo spontaneous mutations at a much lower frequency than others; if this frequency were, say, 10 times lower, the radiation dose necessary for doubling the mutation rate would be correspondingly reduced. If this should apply to man, then the 0.1 r per year would justifiably give cause for worry from the genetic point of view.

One thing emerges clearly, that we know far too little on such an important subject, and that an intense study of it is urgently called for. From what little we do know it would appear that, although the radiation dose from the nuclear explosions carried out so far was too low to have caused much genetic damage, a continuation of the tests at the present scale over a period of many years might constitute a serious genetic hazard.

"CHRONIC APPENDICITIS"

In even the best-conducted hospitals chronic appendicitis is one of the commonest surgical diagnoses. Since treatment is almost invariably by removal of the appendix, allowing not only its immediate careful inspection by the surgeon but its more detailed study by the pathologist later, it would seem reasonable to assume that the diagnosis had long since attained a clear meaning for clinician and pathologist. But this is far from being so, as the correspondence columns of this *Journal* have testified for some months recently; moreover, the writings on this disease (if disease it be) reveal a remarkable dearth of facts about this most ordinary complaint. As Mr. S. H. Wass says in an article at p. 752 of the *Journal* this week: "Some people believe that chronic appendicitis is a clinical entity of common occurrence, others that there is no such disease."

The problem, as it presents to the surgeon, is that of a patient who complains of recurring pain in the right lower quadrant of the abdomen, sometimes sharp, sometimes dull, and occasionally colicky, often associated with vague digestive upset, flatulence, and constipation, accompanied by, as the only positive physical sign, tenderness sharply localized to McBurney's point. Many possible causes immediately suggest themselves, and the surgeon reviews each in turn. As he casts round diligently for an alternative diagnosis to chronic appendicitis the symptoms continue. The patient and his relatives will probably long since have indicted the appendix, and the harassed family doctor may well have hinted at the necessity of having it out. Little wonder then that under the pressure of events the surgeon reluctantly (or not so reluctantly, for many factors influence his decision) feels obliged to explore the abdomen. Having drawn a blank in his search elsewhere he returns to the appendix, and is duly heartened to find it other than normal. Whether it is long (too long) and distended, or shrivelled and fibrous, or kinked or tethered, or infected, or contains a faecolith, it is removed, for removed it must be. The patient is duly informed that the appendix was scarred and better out of the way and is followed through a short convalescence. The case is duly indexed as one of chronic appendicitis, and if the registrar is in any indecision about whether to record the result as "cured" or only "relieved" he knows that no one is likely to quarrel with his verdict either way.

Meanwhile, the problem passes to the pathologist—with the hope that he will find some deviation from normal or, better still, some striking changes which might reasonably explain the symptoms. If he is

[1] Keith, Sir A., *Human Embryology and Morphology*, 1933, 5th ed. London.
[2] Boyd, W., *Surgical Pathology*, 1947, 6th ed., Saunders, Philadelphia.
[3] Hertzler, A. E., *Amer. J. Obstet. Gynec.*, 1926, **11**, 155.
[4] Wilkie, D. P. D., *Brit. J. Surg.*, 1921, **8**, 392.
[5] Pratt, F. W. M., *British Medical Journal*, 1954, **2**, 1352.
[6] Millard, A. H., ibid., 1955, **1**, 230.
[7] Moir, J. C., ibid., 1954, **2**, 1415.
[8] Bourne, A., ibid., 1955, **1**, 45.
[9] McLennan, I., and Watt, J. K., ibid., 1954, **2**, 736.
[10] Wickes, I. G., ibid., 1954, **2**, 869.
[11] Westlake, E. K., ibid., 1954, **2**, 869.
[12] Macfarlane, J. A., ibid., 1954, **2**, 1109.
[13] van Meurs, D. P., ibid., 1954, **2**, 1230.
[14] Ackerman, L. V., *Surgical Pathology*, 1953, London.

honest he will at the outset admit to finding the decision a difficult one, and this for a variety of reasons. First, the appendix is known to change with advancing years,[1] and even the standard textbooks of histology seem at a loss to describe the normal. Secondly, it has undergone the trauma of removal. Thirdly, the pathologist may agree that Boyd[2] was right when he said: "To-day every appendix is condemned by some pathologist somewhere." Little wonder, then, that he often writes a non-committal report which satisfies the surgeon and his own conscience but helps not at all to advance knowledge of the disease.

But when challenged not with the individual case but the general question, Is there such a condition as chronic inflammation of the appendix, and, if so, is it common or rare? the pathologist seems to be more sure of himself.[3] Acute appendicitis he knows and understands. The infection varies in intensity, and its effect is profoundly influenced by the presence of obstruction.[4] When the diagnosis is overlooked or when operation is, for some very good reason, deferred, the acute process may subside and be followed by a resolution which is often remarkable. Inevitably, however, the appendix will carry the scars of this acute infection, sometimes spread diffusely along its length with thickening of the wall and obliteration of the lumen, sometimes limited to one short segment. But, whatever the result, this is not chronic inflammation: it is healed appendicitis. No doubt the same fibrosis can follow recurrent mild attacks of appendicitis; none of them may present clinically as an urgent illness, but the scarring that follows one attack may predispose to the next. Fibrosis obstructing the lumen may also, though rarely, lead to a mucocele or to one or more diverticula. Of the occurrence of "chronic appendicitis," of a continuing low-grade infection with its typical cellular reaction, the pathologist has no experience. If it exists at all it must surely be a rare disease. He knows of no pathological lesion which fits in with the clinician's conception of a "grumbling" infection—that is, apart from tuberculosis, actinomycosis, and the like.

The surgeon, undismayed by the pathologist's incredulity about chronic inflammation, may speak of appendicular colic due to kinks or bands, to obliteration of the lumen, to obstruction by faecoliths,[5 6] or even to hypertrophy of the neuromuscular complex of Masson. Even if he admits that, during abdominal operations for other disorders, he often finds equally abnormal appendixes apparently causing no trouble whatever, and even if he fails to explain away the gynaecologist's challenging comments on the high incidence of the disease in women aged between 15 and 45,[7 8] he can still confidently claim an 80% cure rate following appendicectomy.[9] However, it is too much to claim that this proves the symptoms were due to chronic appendicitis.[10 11] While the 80% may live happily ever after, as do their general practitioners,[12] what of the others? It is not good enough to say that the diagnosis was in error and operation unnecessary (but without much risk). How many of them pass on to later troubles? For the easy diagnosis having been used up by removing the appendix the next surgeon is left to make a fruitless search for adhesions.[13] Surely it is high time for a study to be made of "chronic appendicitis" with a control group of patients treated non-operatively. Until clinical and pathological findings have been carefully compared and analysed, the suspicion is bound to linger among the unconvinced that Ackerman[14] was right when he suggested a change of name from "chronic appendicitis" to "chronic remunerative appendicitis."

ENDOCARDIAL FIBROELASTOSIS IN INFANTS

Endocardial fibroelastosis or sclerosis is not a common condition, but is now well recognized as a cause of death in infancy and very occasionally later in childhood. Its distinctive pathological feature is a thick, white, opaque endocardium in one or more chambers of the heart. The thickening is due to a great increase of fibrous and elastic tissue in the endocardium, with slight fibrosis of the immediately subjacent myocardium in some cases, though not in all. The chambers of the left side are most often affected, especially the left ventricle; the right atrium and ventricle are spared in most cases or are less severely affected.

The condition is encountered either as an isolated lesion in a heart otherwise developmentally normal, or associated with other cardiac anomalies, most often with stenosis or atresia of the aortic or mitral valve, sometimes with an aberrant coronary artery or coarctation of the aorta. In a paper appearing at page 765 of the *Journal* this week, Dr. J. F. Horley has pointed out that the majority of cases of fibroelastosis can be divided into two distinct groups: those associated with aortic valvular lesions and hypoplasia of the left ventricle, in which the infant seldom survives for more than a week or two and the heart is but little enlarged; and those without associated cardiac defects, in which survival for several months is the rule, and the heart is much enlarged owing to dilatation and hypertrophy of the left ventricle. The first type he calls foetal fibroelastosis, because it obviously develops before birth; the second he calls infantile fibroelastosis, apparently on the assumption that it is not congenital but develops after birth.

[1] Gross, P., *Arch. Path.* (*Chicago*), 1941, **31**, 163.
[2] Weinberg, T., and Himelfarb, A. J., *Bull. Johns Hopk. Hosp.*, 1943, **72**, 299.
[3] Ullrich, O., *Z. menschl. Vererb.-u. KonstitLehre*, 1938, **21**, 585.
[4] Johnson, F. R., *Arch. Path.* (*Chicago*), 1952, **54**, 237.

It is doubtful whether this assumption is justified, despite the fact that fibroelastosis without valvular lesions is very rarely seen in infants less than three months old; for it is to be expected that, when fibroelastosis is an isolated lesion, survival will be longer than is likely in the presence of severe valvular or other congenital cardiac anomalies.

The cause of fibroelastosis is not known. Formerly it and the associated valvular lesions were believed to be a result of infective inflammation and were known as "foetal endocarditis." This theory was decisively rejected by P. Gross,[1] who favoured a developmental origin. The histology of the thickened endocardium and stenosed valves gives little support to the infective theory. A genetic origin has been postulated, and this theory gains support from the occasional occurrence of fibroelastosis in siblings, as reported by T. Weinberg and A. J. Himelfarb,[2] and by O. Ullrich,[3] who described the case of triplets, of whom the two identical were affected, and the third, dissimilar, survived. The theory most generally favoured at the present time attributes the condition to anoxia. It was shown by F. R. Johnson[4] that the associated cardiac anomalies are usually such as could cause anoxia of the endocardium of the affected chambers. Horley strongly supports this theory. He quotes reports by other workers to show that, when aortic atresia is accompanied by an interventricular septal defect, which admits oxygenated blood from the right ventricle, fibroelastosis of the left ventricle does not occur, although it invariably accompanies aortic atresia in the absence of such a defect. This theory less satisfactorily explains cases of fibroelastosis without other cardiac anomalies, in which there is no evident cause of anoxia of the endocardium.

Fibroelastosis is not often diagnosed with confidence during life. When other cardiac defects exist with it, these are mainly responsible for the clinical features of the case. When there are no associated anomalies of the heart, the infant often appears to be healthy for some months, and then begins to present clinical evidence of heart failure, the heart is found to be enlarged, and the electrocardiogram is indicative of myocarditis. The onset of heart failure may be surprisingly sudden, and death may follow within a few days. The reason for this severe effect on the myocardium is problematical. Gross postulates that the thickened endocardium interferes with the circulation in the heart wall by obstructing the small vessels that penetrate it to open into the chambers. Histological evidence of myocardial degeneration is seldom impressive, and often the clinical evidence of heart failure and the dilatation of the left ventricle seem disproportionate to the microscopical evidence of myocardial damage.

CLUBBING OF FINGERS

If the shade of Hippocrates reads the medical journals he may be surprised and perhaps gratified by the revival of interest in clubbing of the fingers, a sign which he first described twenty-five centuries ago. He must also feel distressed that his successors have added so little to his own knowledge of the subject. It has now become clear that clubbing of the fingers may be hereditary and of no diagnostic significance, or it may be acquired and signify disease in other parts of the body. Acquired clubbing of the fingers and toes is sometimes said to appear occasionally without any disease being present, but the truth of this assertion may well be doubted because there are so many obscure conditions which may cause it to appear.[1] Indeed, one of the most mysterious features of clubbing is the fact that it is acquired in the course of diseases so different as bronchial carcinoma, congenital heart disease, biliary cirrhosis, lung abscess, and hypothyroidism after thyroidectomy.

In recent years it has been more widely recognized that clubbing of the digits is sometimes only a part of a generalized hypertrophic osteoarthropathy which includes periostitis, synovitis, and painful oedema of the limbs. In the *Journal* this week Drs. T. Semple and R. A. McCluskie report a most interesting series of twenty-four patients in whom this disorder was associated with bronchial carcinoma, a disease which they consider to be the chief cause of the generalized hypertrophic osteoarthropathy. Vogl *et al.*[2] have recently described the same condition in six patients with bronchial carcinoma and one with a chronic lung abscess. The authors of these two papers have described the classical clinical features of the condition, emphasizing the pain, swelling, redness, and tenderness in the limbs, and the stiffness of the joints in association with progressive clubbing and dusky coloration of the tips of the fingers and toes. Hypertrophic osteoarthropathy commonly calls for attention, and sometimes cripples the patient, before the presence of pulmonary disease is suspected. In such cases it is apt to be diagnosed and treated as rheumatoid arthritis without any benefit to the patient. In contrast, the authors of both papers report rapid and dramatic relief of the "rheumatic" symptoms after treatment of the primary pulmonary disease.

While our clinical knowledge of this interesting condition has advanced, we remain very much in ignorance of the nature of the processes which produce such a curious state of affairs. In 1949 it was observed in an annotation in this *Journal*[3] that the subject lends itself to armchair theorizing and that physiological clues were few by comparison with the wealth of clinical data and the numerous hypotheses. The supply of hypotheses has continued to outstrip that of clues, but G. M. Wilson[4] has confirmed the finding of an increased blood flow through clubbed fingers and has shown that this is not due to the action of vasodilator nerves. He also found that treatment of the intrathoracic disease was

[1] Leopold, S. S., *The Principles and Methods of Physical Diagnosis*, 1st ed., 1952, p. 356, Philadelphia.
[2] Vogl, A., *et al.*, *Amer. J. Med.*, 1955, **18**, 51.
[3] *British Medical Journal*, 1949, **1**, 228.
[4] Wilson, G. M., *Quart. J. Med.*, 1952, **45**, 201.
[5] Jack, G. D., *Trans. med.-chir. Soc. Edinb.*, 1952, **132**, 75.
[6] Jackson, W. P. U., *British Medical Journal*, 1949, **1**, 216.

followed by a decrease in the peripheral blood flow and a retrogression of the clubbing. An increase in blood flow cannot be the whole explanation, because clubbing is not a feature of hyperthyroidism, in which there is an increased peripheral circulation, but it does appear in some cases of myxoedema, in which the peripheral blood flow is presumably sluggish. Wilson has suggested that the important factor is a blood supply in excess of metabolic requirements, and this may explain some of these apparent anomalies.

Whatever the cause of hypertrophic osteoarthropathy, it is important that the condition should be recognized, because it may be the first clue to the presence of a bronchial carcinoma, and anything which may enable an early diagnosis to be made of this disease is to be welcomed. Moreover, Vogl *et al.* consider that the condition itself is often so distressing and disabling that resection of a bronchial carcinoma may be justified by the relief of symptoms even if it does not eradicate the malignant disease. It is well to remember, however, that G. D. Jack[5] found only three fully developed cases of hypertrophic osteoarthropathy in 668 patients with bronchial carcinoma and that it took Semple and McCluskie seven years to find twenty-four cases. It is also worth while recalling W. P. U. Jackson's warning[6] that the combination of a cough and clubbing of the fingers does not by itself justify the diagnosis of a serious pulmonary disease, though it should certainly encourage further investigations.

EPILEPSY AND SCHIZOPHRENIA

In their interesting article on psychical phenomena in temporal lobe epilepsy at p. 748 of the *Journal* this week Drs. S. Karagulla and Elizabeth Robertson draw a number of parallels between these symptoms and those experienced by the schizophrenic patient. They principally concern themselves with hallucinations, taking this term to cover a wide range of abnormal experience. At one end is the disembodied thought, which may be formless and more a subjective experience of something going wrong in the process of thinking. This was observed in an epileptic, and was exactly reproduced by electrocortical stimulation in a strictly localized region of the right temporal lobe. It closely corresponds in form with familiar complaints by schizophrenic patients—for example, of forced thinking, of thoughts being inserted into the mind by an outside agency, or of thoughts getting crossed. In the middle of the range are hallucinatory phenomena, which are experienced as coming from within. Schizophrenics commonly report that they hear a voice coming from some particular part of the body, not infrequently the abdomen; and the authors parallel this with the experience of a 7-year-old epileptic boy, who felt something talking in his stomach as an accompaniment of the abdominal sensations which are such a frequent part of the aura of an epileptic attack fired off from a temporal focus. Finally there are the completely exteriorized hallucinations, and here the similarities are not quite so close. The schizophrenic remains at all times aware of an external reality, and even when auditory or visual hallucinations seem to him to take place in this external world he usually reports that they have a lesser or different quality of reality than actual objects and events. The pseudo-reality of the epileptic hallucination is often more real than this, as in the case reported in which the patient was blind to everything else.

There are other symptomatic differences between abnormal psychic experiences in the epileptic and in the schizophrenic. Whether the epileptic suffers from a hallucination in isolation, or as part of the aura which precedes a major convulsion, consciousness is usually to some extent clouded or altered. Probably many significant epileptic experiences never come to the notice of the doctor because subsequent memory for them is obliterated. Even when it is retained it may be incomplete. Any demonstrable alteration of consciousness is rare in the hallucinated schizophrenic, although for other reasons he may not be completely in touch, or be unable to give a clear account.

However, it is not only in hallucinations that striking similarities exist between the experiences of the epileptic and of the schizophrenic. A feeling of unreality, sudden, overwhelming, but of brief duration, is extremely suggestive of a temporal lobe attack. Similar feelings, of a more persistent nature, occur in a variety of psychiatric syndromes, but with particular frequency in the early stages of schizophrenia. Sudden changes of mood, depression, panic, ecstatic states, and moods with an other-worldly quality occur both in epilepsy and in catatonic schizophrenia. The *Wahnstimmung*, or state of mind in which everything that is going on seems to have some mysterious significance, or to have some special reference to the patient, is a common and characteristic feature of oncoming paranoid schizophrenia, and is almost as frequently observed in the twilight state which may succeed a closely spaced series of fits or accompany petit mal status. As long ago as 1936 H. W. Gruhle,[1] who was one of the pioneer workers on the psychopathology of schizophrenia, pointed out that there was no phenomenological difference between the form of the primary delusion in schizophrenia and in epilepsy. There are patients in mental hospitals, diagnosed as schizophrenic, who have fits from time to time and even die in status; we may be quite sure that some of them are unrecognized epileptics.

The work of Karagulla and Robertson owes a large part of its interest to the fact that precisely defined and complex psychic experiences could be produced by electrocortical stimulation in a narrowly circumscribed locus in the brain of the conscious subject. This was the work of Wilder Penfield, under whom one of the authors has worked in the department of neurology at McGill. Success in the surgical treatment of epilepsy, a field in which Penfield is the outstanding pioneer, would seem to depend largely on localizing the epileptogenic focus by direct stimulation under local anaesthesia; and neurosurgeons who forgo the advantages of

[1] Gruhle, H. W., *Z. ges. Neurol. Psychiat.*, 1936, **154**, 395.

this technique are neglecting an important aid to localization. The particular moral which Karagulla and Robertson draw from their work, that the phenomenological similarities between epilepsy and schizophrenia are so striking as to merit further intensive study, should also arouse interest and attention.

DANGERS OF MERCURY

Growing appreciation of the importance of enzymes in relation to the action of chemotherapeutic drugs has advanced—and is advancing—rational therapeutics, and gradually the days of traditional and empirical therapy are passing away. Although the scientific approach to treatment has been chiefly concerned with the infections, it shows no signs of stopping there; the times are propitious to investigating whether the old remedies do all that they are supposed to do. One at present the subject of discussion is mercury—a time-honoured recipe for infants both in the form of calomel and as hydrarg c. cret. (grey powder). Is there any good evidence that either of these preparations is of any value? If not, they should surely be removed from the pharmacopoeia.

Constipation in their infants has been a bugbear to mothers for generations and a "corrective" or laxative is administered to treat and even to prevent the condition—and also to a greater or less extent as a panacea. Any unexplained fever or out-of-sorts state is apt to be treated similarly. Many children are still given a regular weekly laxative—like a talisman to ward off evil things. Teething has naturally been a fruitful subject for catharsis. Some parents attribute any intercurrent upset between the ages of 4 months and 2 years to teething, and administer "teething powders." Are teething powders, of any sort, ever necessary? Teething is a physiological phenomenon like menstruation and pregnancy, and like them it may occasionally become pathological, but undoubtedly less often. Nearly all teething powders contain a laxative, yet there is no evidence that the process of dental eruptions is associated with constipation or that calomel is a febrifuge. Parents should be informed that teething is normally a natural process and that nature seldom requires assistance. If an infant is so upset as to require some treatment he should be seen and treated by the doctor, not by the chemist or grocer, who will undoubtedly continue to supply proprietary remedies if parents continue to demand them. But has the time not come to question the need for grey powders in any disorder?

Mercury is a dangerous drug, especially in infancy, and some doctors have come to consider that it should not be prescribed for internal administration in any form. The Minister of Health is "considering urgently" whether grey powders should cease to be issued from child welfare clinics.[1] If a laxative is necessary, more effective and innocuous preparations are available, such as syrup of figs or syrup of senna. Castor oil is now generally regarded as a grave risk for children, and, happily, tragedies from peritonitis due to rupture of an inflamed appendix, as a result of the violent peristaltic contractions produced by castor oil prescribed for a stomach-ache, are much rarer than they used to be. Now that the ill effects of mercury are becoming clearer, a diminution in the incidence of such pathological conditions as pink disease may be hoped for; indeed, there is already some evidence that this is happening.

[1] *Evening Sentinel*, March 15.

ROYAL SOCIETY'S NEW FELLOWS

Among the 25 new Fellows of the Royal Society elected on March 17 are three members of the medical profession as well as several scientists whose work has contributed to the advancement of medicine. Professor A. W. Downie, one of the leading authorities on the viruses that cause human disease, is specially noted for his work on the smallpox and related viruses. He has been professor of bacteriology at Liverpool University since 1943, and before that was at the National Institute for Medical Research. Professor K. J. Franklin, of St. Bartholomew's Hospital, has been professor of physiology in the University of London since 1947. His investigations into foetal and renal circulatory systems have been notable for the ingenious techniques, including cineradiography, that he and his collaborators have used. A classical scholar, Professor Franklin has also made distinguished contributions to the study of medical history; his biography of the late Sir Joseph Barcroft appeared two years ago. Sir Harold Himsworth, secretary of the Medical Research Council since 1949, was formerly professor of medicine at University College Hospital Medical School, where his investigations were concerned chiefly with diabetes mellitus, the thyroid, and liver disease. It is good to see clinical research thus honoured in the person of one who has early exercised a great influence on medicine. Since becoming secretary of the M.R.C. Sir Harold has naturally played an important part in the organization of the clinical trials that in recent years have made the Council's work of such unique value to the advancement of rational therapeutics. Dr. D. J. Finney, though director of the Agricultural Research Council's unit of statistics, is well known to many medical men for his development of the statistical methods commonly used in pharmacology, and especially in the assay of biological preparations. Mr. A. F. Huxley, assistant director of research in physiology at Cambridge, has made important contributions to knowledge—in a school renowned for its neurophysiology—about the conduct of impulses in nerves and muscles, latterly with the aid of the interference microscope. Professor O. E. Lowenstein, Mason professor of zoology and comparative anatomy in the University of Birmingham, has been elected for his work on the comparative physiology of the vertebrate labyrinth. Professor G. P. Wells, as professor of zoology, University College, London, comes closely into contact with the medical student in his formative years.

EMERGENCIES IN GENERAL PRACTICE

ACUTE RESPIRATORY OBSTRUCTION

BY

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Acute respiratory obstruction ranks high on the list of emergencies in which prompt action is necessary to avert disaster. Unfortunately, in some cases the emergency arises so suddenly that death ensues before medical aid can be summoned; but in most cases the obstruction is more or less slowly progressive, giving time for preventive measures at all stages of its development.

Obstruction of the Nose, Mouth, and Pharynx

Lesions in the nose very rarely cause severe obstruction. Some years ago, however, a newly born infant was admitted to St. Bartholomew's Hospital in such respiratory distress that it had to be placed in an oxygen tent. A very large polyp in the left anterior nares completely blocked both nasal passages. Removal of this obstruction gave immediate relief to the distress, respiration at once becoming normal, and remaining so.

The mouth and pharynx provide a number of cases. A large foreign body—for example, a bolus of food—may be inhaled in the deep inspiration of pertussis, completely blocking both food and air passages. The foreign body should be hooked out with the index finger; in infants the retching induced by this manœuvre often proves most effective. During anaesthesia, and in unconscious states following traffic and other accidents, the lower jaw and tongue may fall back, causing an exactly comparable obstruction. The jaw must be held forward and an airway inserted or the tongue drawn out with a tongue clip.

Acute inflammatory conditions which give rise to gross obstructive swelling include retropharyngeal abscess, usually in young children, and, rarely, lingual abscess. If seen early vigorous treatment with penicillin injections, from 100,000 to 500,000 units twice daily, should be begun, and in most cases the condition will abort. If the response is doubtful, one of the other antibiotics should be substituted: 2 g. of chloramphenicol daily in divided doses for adults, with proportionally smaller doses six-hourly for children depending on their weight; for children the palmitate emulsion is preferred, each drachm (3.5 ml.) containing 125 mg. of chloramphenicol. Alternatively, chlortetracycline ("aureomycin") or oxytetracycline ("terramycin") may be used in half the above dosage. If an abscess has already developed it should be incised. No general anaesthetic is advisable, and it is very doubtful if topical cocaine has any real effect. The child should be laid supine on a table with a sandbag under its shoulders and the retropharyngeal abscess incised. The child should then be picked up by the feet so that the released pus runs from its nose and can be aspirated by a sucker.

Quinsy does not, as a rule, cause much respiratory obstruction unless oedema has spread downwards to the glottic opening. This abscess may be evacuated by the classical stab in the soft palate or, better still, by sharp-pointed sinus forceps passed up along the supratonsillar fossa. If a general anaesthetic seems imperative a non-irritant vapour—for example, chloroform—would be indicated, the patient being placed as for tonsil dissection.

Allergic swelling of the mouth and tongue may follow a wasp or bee sting on the back of the tongue; usually when the insect has been accidentally swallowed with a drink. Or it may be a manifestation of recurring attacks of angioneurotic oedema or of anaphylaxis in serum disease. In a patient sensitive to penicillin it has followed the introduction of a penicillin cone into a tooth socket after dental extraction. In all such cases the swelling may extend to and involve the larynx.

In severe or rapidly progressive cases the intravenous injection of 5 to 15 minims (0.3–0.9 ml.) of 1 in 1,000 adrenaline hydrochloride will usually control the swelling. If not, laryngeal intubation or tracheotomy should be performed without further delay.

Laryngeal Intubation and Tracheotomy

The choice between intubation and tracheotomy depends on several factors: the instruments available; the probable duration of obstruction; the need for suction in the after-treatment; and the experience of the practitioner. Intubation is indicated in cases of temporary obstruction. Tracheotomy should be performed if the obstruction is likely to last longer than 24 hours; another reason for it is that aspiration is easy to apply through the cannula. Tracheotomy is therefore often used in prolonged states of coma following head injuries, and sometimes in bulbar poliomyelitis. In the minds of older practitioners tracheotomy is associated with laryngeal diphtheria. But since the immunization campaign, begun in 1940, this disease has practically disappeared in Britain. Dr. William Gunn, physician in charge of the infectious diseases department of the Royal Free Hospital, in a personal communication confirming this, states that croup also has virtually disappeared, whether occurring idiopathically or associated with other diseases, notably measles. Nowadays, therefore, the young doctor is unlikely to get much experience of tracheotomy, but he should have had much practice in direct laryngoscopy during his anaesthetic clerking.

The important points in direct laryngoscopy are to have the patient's neck flexed at its lower end and extended at its upper end; and to lift the tongue and epiglottis with the blade of the laryngoscope, and not use the instrument as a lever with the upper teeth as fulcrum. Intubation is effected by direct laryngoscopy. The patient is laid flat on a table and the neck flexed forward at its lower end and extended at its upper end. If the mouth cannot be opened because of spasm this may be overcome by the intravenous injection of 50 mg. of suxamethonium chloride. The handle of the laryngoscope is held in the left hand, while the fingers of the right hand retract the upper lip to prevent its being nipped on the teeth. The blade of the laryngoscope is advanced along the dorsum of the tongue in the midline until the tip of the epiglottis is seen; it is then advanced for just over 1 cm. in a child or 2 cm. in an adult. The laryngoscope is then lifted sufficiently to take the whole weight of the patient's head and the glottis comes into view. As soon as he takes a deep breath the glottis opens, and the endotracheal tube, which is held ready in the right hand, is quickly passed between the cords. Care must be taken to *lift* the blade, never to use it as a lever with the upper teeth as fulcrum.

For the operation of tracheotomy the patient should be supine, a small sandbag under the shoulders, and the head well extended. The table should be tilted, with foot down, and oxygen given through a mask. An assistant should hold the head, neck, and chest in a straight line. In semi-urgent cases the neck may be infiltrated with local analgesic; in urgent ones no analgesic should be used. The thyroid and cricoid cartilages are grasped with the thumb and middle finger of the left hand, and an incision made, exactly in the midline, from the lower border of the thyroid cartilage almost to the suprasternal notch. This is deepened, bleeding points being ignored, until the corrugated anterior surface of the trachea is felt with the left index finger. This is then

opened by a stab through the second and third tracheal rings—dilators are introduced and the cannula is then passed. If time permits it is better to divide the isthmus of the thyroid gland between clamps, and then excise a circular disk from the anterior tracheal wall at that level. Finally, do not suture the wound too close to the tube, or surgical emphysema may result; and on no account open the trachea through the first ring, as this usually causes a permanent stenosis of the larynx. Difficulties are met if the head, neck, and chest are not kept strictly in line, and if a hasty stab in the trachea is allowed to close before dilators are introduced. Then, especially in infants, the tube may be forced into the fascial planes anterior to the trachea, or between the anterior tracheal wall and its mucosal lining. It needs stressing, however, that if penicillin is given in adequate dosage in the early stages of acute throat infections most of these emergencies will be avoided.

Laryngeal Obstruction

The larynx is by far the most frequent site of obstruction. The loose attachment of the lining epithelium to the underlying structures, especially in the aryepiglottic folds and over the arytenoid and corniculate cartilages, favours the rapid development of gross oedema in these situations. In childhood the larynx is relatively small in proportion to body size, the cartilages are more pliable, the mucosa less closely adherent, and its lymphatic drainage more plentiful than in the adult. Thus acute symptoms are much more readily produced in children. A slowly increasing constriction of the glottic aperture is much more readily tolerated than one which is rapidly progressive.

Foreign Bodies

The familiar condition of "food going the wrong way" produces a temporary spasm for which only the time-honoured slap on the back is necessary. A larger foreign body—for example, food inhaled during the inspiratory phase of coughing—may block the glottis completely or cause marked glottal spasm. If a laryngoscope and laryngeal forceps are immediately available the foreign body should at once be removed. If asphyxia threatens it is better to perform an emergency tracheotomy first.

Vomit or blood may enter the larynx during induction of anaesthesia and, especially when thiopentone is being used, set up severe spasm. The anaesthetic should be stopped and the foreign matter sucked out. A muscle relaxant—for example, suxamethonium chloride, 50 mg.—may be given intravenously, thus permitting the passage of a laryngoscope and, through it, an endotracheal tube. Among other foreign bodies must be mentioned the membranes of laryngeal diphtheria and of acute laryngo-tracheo-bronchitis. These may have to be removed by laryngeal forceps, following preliminary tracheotomy.

Swelling of the Laryngeal Walls

Swelling of the laryngeal walls may be due to one of the following:

Local or Adjacent Infection.—In infants an acute laryngitis may produce alarming symptoms, even to the point of needing tracheotomy. Perichondritis may follow trauma or irradiation and may complicate syphilis, tuberculosis, carcinoma, typhoid, diphtheria, and many of the specific fevers of childhood. Treatment should be directed to the primary cause if possible. Complete rest of the patient and larynx, full doses of penicillin or other antibiotic in the primary form, and tracheotomy if signs of serious obstruction develop are the appropriate measures. If an abscess develops in the larynx it should be evacuated through the laryngoscope. In Ludwig's angina full doses of penicillin may suffice to abort the infection, but if in spite of this the condition worsens incision in the midline of the neck and drainage are employed. Tracheotomy may be necessary if asphyxia threatens.

Trauma.—This may be mechanical, as in traffic accidents or following a high tracheotomy or clumsy instrumentation, or it may take the form of scalds, as in children drinking from the spout of a teapot or hot kettle, or of burns from inhaling flames in petrol fires or from inhaling caustic fumes in industry. In accident cases early tracheotomy is indicated if obstruction is marked and there is a possibility of intralaryngeal haemorrhage. In the other cases strict rest in bed, administration of oxygen, and sedatives to reduce the cough are usually sufficient. A careful watch must be kept for signs of impending asphyxia, a tracheotomy set being ready for instant use.

Allergy.—This has already been described in connexion with the mouth and pharynx, together with the appropriate treatment.

Oedema Associated with General Disease.—This occurs, for example, in nephritis, cardiac failure, and idiosyncrasy to iodides.

Neoplasms.—Innocent growths causing serious obstruction are rare. Malignant growths are a much commoner cause, but usually only at a late stage, when they would be the responsibility of the laryngologist. Should the general practitioner have to perform tracheotomy he should make it as low as possible in order to be clear of the growth.

Spasm

Spasm of the sphincter or paralysis of the dilators of the glottis may cause laryngeal obstruction. Spasm may be of central or peripheral origin. Possibly the commonest cause is the induction of anaesthesia, especially with ethyl chloride or ether and, as previously mentioned, with thiopentone. The anaesthetic should be stopped, oxygen administered from the anaesthetic machine, and the bag squeezed when the glottis opens. Alternatively the glottis may be watched through a laryngoscope and quickly intubated as soon as it opens.

In infants congenital laryngeal stridor, which is present night and day, and laryngismus stridulus, which may wake the infant from sleep, occasionally occur. The former causes alarm to the parents, but no great dyspnoea; the latter causes momentary but severe dyspnoea and is treated by sitting the child up, slapping its back, making it sneeze, or hooking its tongue forward with a finger. Both conditions disappear in the first few years of life.

In adults spasm may be hysterical, due to local irritation of the recurrent laryngeal nerve, or of central origin, as in tabes and tetanus. During an attack an ampoule of chloroform or amyl nitrite should be crushed by the patient and the vapour inhaled. Otherwise sedatives are given. Bilateral abductor paralysis is usually due to bulbar lesions, but may be due to pressure on, or severe injuries of, both recurrent laryngeal nerves, as after thyroid gland operations. In an established bilateral paralysis phonation is good, and quiet respiration is possible, but on exertion severe dyspnoea may develop. When no recovery can be expected the choice of treatment is either permanent tracheotomy, with the use of a tube having an expiratory valve, or operation permanently to abduct the posterior part of one cord.

In the diagnosis of these various causes of laryngeal obstruction the history and symptoms are important, but only inspection by mirror, or by the direct method in children, will establish it with certainty. In some cases time will not permit of this inspection. Obstruction sufficient to call for immediate operation is shown by recession at the suprasternal notch and epigastrium, stridor, and restlessness. Cyanosis is late, ashen pallor being more usual. Jackson stresses the importance of recognizing the cause of restlessness in obstruction, lest morphine be given in error, with disastrous results.

In all these cases urgent action is required. It is always better to operate before it is strictly necessary than to delay until it is too late.

Next article on Emergencies in General Practice.—"Agricultural Pesticides," by Dr. E. F. Edson.

Nova et Vetera

SIR THEODORE TURQUET DE MAYERNE 1573–1655

Quid de Mayernio plura?
Mayernium dixeris, omnia dixeris.

So wrote Mayerne's godson, Sir Theodore de Vaux, in the course of a long eulogy for the tombstone in St. Martin-in-the-Fields when Mayerne was buried there 300 years ago. He had died at the age of 82 after a full life, in the course of which he had been physician to four monarchs and had initiated the incorporation of two City companies.

Mayerne's father was a French Protestant and a celebrated writer of history. After the Massacre of St. Bartholomew in 1572 he had fled to Geneva, and it was here that his son Theodore was born in the following year on September 28. Mayerne received his early education in this city, and a classbook of his, which still survives and contains annotated drawings of vessels used in distillation, reflects his early interest in this subject.

From Geneva, Mayerne went to Heidelberg, where he spent four years at the university before going on to Montpellier. It was about this time, when he was only 19, that Mayerne published his first book.[1] It seems to have excited little comment, although in a letter to Humphrey Milford dated March 31, 1919, deploring the lack of a really satisfactory motor road-book, Osler writes: "[There is] not one to be put in comparison with that of my friend Theodore de Mayerne, who . . . issued one of the first and the best in Europe."[2]

It was probably due to Riverius, first physician to King Henry IV of France and professor of medicine at Montpellier, that Mayerne went to Paris after graduating M.D. in 1597, and was appointed one of the king's physicians. In his medical practice he made considerable use of chemical remedies, which were then regarded as an innovation, and in consequence brought upon himself the condemnation of the College of Physicians of Paris (1603). This doubtless influenced his eventual removal to England, where his reception contrasted favourably with his experiences in Paris, so that some years later, in a letter to his friend Sir William Paddy, Mayerne wrote: "[Thou] didst not look upon me with blear and swoln eyes with the viporous venome of envy; but thou didst entertain me, being a stranger, candidly and with a cheerful countenance. . . ."[3] He had been incorporated M.D. at Oxford and appointed physician to the queen on his first visit to this country in 1606. He returned in 1611 after the assassination of Henry IV, and within the space of a few years was appointed first physician to the king and elected Fellow of the College of Physicians.

Power over Distillation

He soon became involved in the preparation of the first edition of the *Pharmacopoeia Londinensis*, in which he is said to have had the assistance of a French Huguenot chemist. Could this have been Gideon de Laune, who, with Mayerne, had so much to do with the founding of the Society of Apothecaries in 1618? Their first charter gave them in theory complete power over distillation of all kinds, but twenty years later, following the incorporation of the distillers, this view was challenged by Mayerne, who contended that the apothecaries were limited (or intended to be) to the preparations in the *Pharmacopoeia Londinensis*. Mayerne had been largely responsible for the promotion of the new company, and for their guidance had assisted Dr. Cademan in the publication of *The Distillers of London* . . . (London, 1639).

Mayerne had been knighted in 1624, and on the accession of Charles I was appointed his first physician, and physician to Queen Henrietta Maria. Aikin seems to think that he made himself acceptable and necessary to successive queens by condescending to matters beneath the dignity of his profession, such as the preparation of "cosmetics of every kind, pastes, lotions, dentifrices, sweet bags, hair powders and the like."[4] Here, however, Aikin may be doing less than justice to Mayerne's preoccupation with chemical and other experiments, as a result of which he brought calomel into use and discovered the purple colour necessary for the carnation tints in enamel painting.

In 1634 Mayerne had at last succeeded in arranging for the publication of Muffet's *Insectorum sive minimorum animalium theatrum*. The manuscript had been offered to him by Darnellus, apothecary to Muffet, who had died in 1604. The explanation of the delay in publication has a curiously modern ring, and makes one speculate about the conditions under which Mayerne worked, for he says:

"It lay for some years in my Study cast aside in the dust among Worms and Moths; truly it was not fault of mine, but of the Printers who were so greedy of Money, that though in many Countreys I invited them by my Letters, and did solicit them to receive the Orphan, yet they refused (as they said) to take upon them an unthankful business; they were not pleased with the benefit of a noble Art, unless it would pay more than the fraight. O the times wherein the pains of learned men are valued at the price the work will be sold for, and the money that must be laid out for ink and paper. . . ."[2]

Mayerne is known from his portraits to have been very corpulent; it is said that he kept no regular meals, but that he had his table constantly covered so that he could eat whenever he found himself disposed. After the execution of Charles I in 1649, Mayerne was appointed nominal first physician to Charles II, and about the same time, perhaps owing to ill-health, he retired to Chelsea, where he died seven years later on March 22, 1655, from the effects of drinking bad wine.

L. M. PAYNE.

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Reports of Societies

LOCAL MEDICAL SOCIETIES

Joint Meeting of Manchester Medical Society and Liverpool Medical Institution

Speaking at the joint meeting in Manchester on March 2, Professor A. W. DOWNIE discussed the relationship of chicken-pox to herpes zoster. The association of chicken-pox with zoster was well recognized, he said, in that child contacts of zoster cases not infrequently developed a clinical infection indistinguishable from chicken-pox. Yet, because of the difference in clinical picture and pathology, in age and seasonal incidence, there had been in many quarters some hesitation in accepting the thesis that zoster is an infection with varicella virus. Three different views appeared to be held: (i) that one virus causes the two conditions, (ii) that the two clinical entities are due to different but closely related viruses, and (iii) that some cases, but only some cases of zoster, are caused by varicella virus. The recent investigations of Hope Simpson in one of the Shetland Isles seemed to show conclusively that the chicken-pox derived from zoster cases is in no way different from ordinary chicken-pox. The clinical picture, interval between serial cases, and infectiousness were the same, and an attack of the one kind of chicken-pox conferred immunity to the other. The experimental infections of children with zoster vesicle fluid by Kundratitz and by Bruusgaard showed that such infections sometimes resulted in clinically typical chicken-pox with subsequent immunity to further inoculation with vesicle fluid from zoster or chicken-pox cases.

Laboratory investigations had been hampered by lack of susceptible experimental animals, went on Professor Downie, but such information as was available had shown no differences between the virus from chicken-pox and that from zoster patients. The histological features of the skin lesions were the same; by electron microscopy the virus particles were identical; and they were agglutinated by convalescent serum from either type of case. Antigen in vesicle fluids cross-reacted completely in complement-fixation tests with convalescent sera. The laboratory findings thus supported the clinical and epidemiological observations that zoster is a particular kind of infection with varicella virus.

Canal Zone

A clinical meeting was held at the British Military Hospital, Fayid, Canal Zone, Egypt, on February 28, at which paediatric cases were shown and discussed. Dr. B. E. SCHLESINGER, Hon. Consultant in Paediatrics to the Army, was among those present.

Preparations and Appliances

TWO GYNAECOLOGICAL INSTRUMENTS

Mr. H. H. FOURACRE BARNS, surgeon, the Hospital for Women, Soho Square, London, W.1, writes that he finds the two instruments illustrated below of great use in his work.

Vaginal Clamp for Radical Hysterectomy.—It is desirable to obtain a watertight cuff of the vagina below the cervix when carrying out a radical hysterectomy for carcinoma of that organ. In order to obtain this vaginal cuff, the clamp illustrated has been made by John Bell and Croyden. The shank of the clamp is angled to the jaws at a right angle,

Hysterectomy clamp.

so that the handle lies comfortably to one side of the uterus when applied to the vagina, application being made from the side. The ends of the jaws are curved to facilitate cutting across the vagina below the clamp. The jaws are heavy and grooved at right angles to the direction of the shank so as to prevent any slipping on the vaginal tissues.

Intrauterine Forceps.—In order that the cervix need not be dilated to a high degree for the introduction of intrauterine forceps, especially in the elderly, the forceps illustrated have been made by John Bell and Croyden. The small width of the blades (¼ in.—6.3 mm.) and joint ($\frac{5}{16}$ in.

Uterine forceps.

—7.9 mm.) allows easy introduction through the moderately dilated cervix. In addition, the joint is situated at a distance from the ends of the blades so that it lies in the middle of the cervical canal of the normal-sized uterus. This allows the blades to be opened for a distance of 1 in. (2.5 cm.), when the cervix is dilated sufficiently to allow the forceps to be passed.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Chlorpromazine Jaundice

SIR,—Your correspondents Drs. J. G. Macarthur and Bernard Isaacs (*Journal*, September 25, 1954, p. 754) plead for more detailed clinical and histological study of cases of jaundice occurring during chlorpromazine therapy. Their plea has every justification, as the drug is among the most frequently prescribed and the incidence of jaundice occurring during its administration is by no means negligible. Chesney[1] (1954) reports two cases from one general practice, and it occurred in 3 of 18 patients treated by Eagles.[2] Other writers record a lower incidence. Thus, jaundice occurred in 3 of 71 patients treated by Lehmann and Hanrahan,[3] 3 of 142 given the drug by Winkelman,[4] and in 6 of 500 observed by Boardman.[5] Other cases have also been reported by Elkes and Elkes,[6] Lancaster and Jones,[7] Zatuchni and Miller,[8] and Van Ommen and Brown.[9] We have recently had the opportunity to study a patient who developed jaundice whilst taking chlorpromazine, and are therefore reporting our findings in your columns.

He was a pattern-maker of 48, of temperate habit, who had never had any physical illness and who was given 25 mg. chlorpromazine ("largactil") thrice daily for a long-standing obsessional neurosis. After he had been taking the drug for three weeks he felt feverish over a period of 48 hours, and during the subsequent three days had some vague abdominal discomfort, so he reported to his doctor, who noted that he was jaundiced. The chlorpromazine was stopped, and the patient ceased work and went to bed. During the subsequent ten weeks he remained in bed at home, afebrile, eating well and without pain or dyspeptic symptoms, but deeply jaundiced, suffering much pruritus and with acholic stools and bile in his urine. The only abnormality on physical examination was an enlarged liver which was neither irregular, hard, nor tender. Although it was thought that the jaundice was due to the chlorpromazine therapy, in view of its protracted course he was admitted to hospital for fuller assessment.

The liver function tests showed the pattern of obstruction (see table), the blood count was normal, the stools were negative for occult blood, barium studies of the oesophagus, stomach,

	Weeks After Onset of Jaundice				
	10	12	13	14	15
Serum albumin g./100 ml.	4·0	3·5	4·5		4·2
Globulin "	2·4	2·3	2·2		2·3
Gamma globulin "alcohol g./100 ml.	0·05	0·05	0·1		0·2
$(NH_4)_2SO_4$ g./100 ml.	1·8	1·5	1·9		1·1
Cholesterol free mg./100 ml.	162	180	190	140	180
Ester "	162	175	270	370	320
Serum alkaline phosphatase units (Jenner and Kay) /100 ml.	19·6	22·8	43·4	36·0	10·5
Bilirubin mg./100 ml.	9·2	6·7	3·0	1·9	1·7
Prothrombin %	60	100			
Zinc sulphate:					
Turbidity (units)	1·0	1·0	2·0		2·0
Flocculation	Negative	Negative	Negative		Negative
Cephalin cholesterol	"	"	"		"
Thymol turbidity (units)	0·5	0·5	1·0		0·5
Flocculation	Negative	Negative	Negative		Negative
Colloidal gold:					
Patterson	2	2	1		2
Maclagen	Negative	Negative	Negative		Negative

duodenum, and small and large intestines were all normal, and the chest radiograph was clear. The blood Wassermann was negative.

In view of the undue persistence of the jaundice as compared with all other recorded cases (except the fatal case reported by Boardman[5] and the two cases of Van Ommen and Brown,[9] which have since been published), it was thought advisable for him to have a laparotomy in case a growth was present, especially in view of the absence of evidence of parenchymatous damage in the liver function tests. Laparotomy was therefore carried out by Mr. Gourevitch. The gall-bladder and common bile duct were not dilated, the pancreas was normal, and there was no evidence

of extrahepatic biliary obstruction, but there were some large soft glands in relation to the common bile duct and the liver was rather pale and its surface granular. A liver biopsy was taken and the abdomen closed. Histological examination showed bile thrombi in the bile canaliculi but no dilatation of the bile ducts, gross perilobular fatty degeneration of the liver cells and slight periportal round cell infiltration but no necrosis of liver cells, no regeneration, no fibrosis, and no reticulin formation. The laparotomy upset the patient very little, and since operation the jaundice has steadily faded, but a trace is still evident and the liver function tests are still abnormal (see table) 15 weeks after the onset of illness. The only treatment given has been a high-protein diet and vitamin supplements.

The histological findings in this case accord very closely with the only other detailed pathological report,[4] and the biochemical changes are similar to those found by Elkes and Elkes,[6] Boardman,[5] Zatuchni and Miller,[8] and Van Ommen and Brown,[9] each of whom reported liver function tests showing an obstructive pattern and normal flocculation tests.

Three points are thought to require emphasis: (1) Chlorpromazine appears to be capable of producing a toxipathic hepatitis characterized by damage to the cells at the periphery of the lobule, blockage of the canaliculi by bile thrombi, and periportal cellular reaction. (2) The liver function tests in such cases show an obstructive pattern without evidence of parenchymatous damage. (3) The jaundice may last for several months.—I am, etc.,

Birmingham, 15. A. G. W. WHITFIELD.

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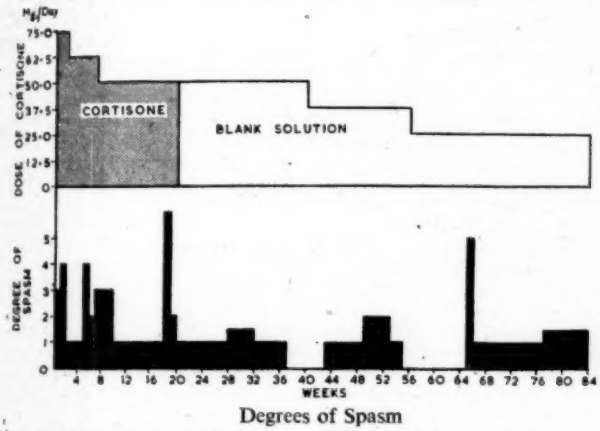
Cortisone, A.C.T.H., and Asthma

SIR,—My two-and-three-quarter years' experience of 47 severe asthmatics treated with cortisone and/or an indistinguishable blank substance does not support Dr. H. Herxheimer's enthusiasm (*Journal*, February 12, p. 416), but is in keeping with your annotator's cautious summing up of



Degrees of Spasm

1—One to two attacks daily, easily relieved } full activities.
2—More than two attacks, easily relieved }
3—Spasm on exertion, free at rest.
4—Spasm on exertion plus attacks at rest.
5—Status asthmaticus.

the present position (*Journal*, January 22, p. 216). In status asthmaticus I have seen cortisone fail in high dosage, and the reports of fatal anaphylaxis after A.C.T.H. injections cannot be lightly cast aside.

My results in the long-term control of asthma with cortisone have not yielded a "high percentage of pronounced improvements." Fifty per cent. is the highest I can claim, and this will fall when the figures from a current blind trial are all included. Certainly, cases have been raised from a life of semi-invalidism to near normality; unfortunately this is not the invariable response. Success and failure in all types of asthmatics, with a wide age range, has occurred. At present it is impossible to foretell the long-term result in any given case, though emphysematous patients with a low respiratory reserve gain no benefit.

The effects of any treatment are difficult to assess in asthmatics, who are so open to suggestion. It is chastening at the conclusion of a blind trial to find that the successful case had been taking the blank solution and the failure cortisone. It is such observations as these which make me echo "*sub judice*" with your annotator. The chart shows the course of a difficult case—the patient still swears by "cortisone," being unaware that he is on a blank solution. That trials should be blind is surely a very happy remark.

It is true that side-effects are not usually severe, but considerable weight gain due to fat or fluid retention must be balanced by material improvement if treatment is to be justified. I shall strongly "discourage its use," except in the most carefully chosen cases. Dr. Herxheimer is enthusiastic; I was much more so a year ago than I am now. Cortisone may soon be freely available; it is very expensive, not without risk, and the results vary. Let us ensure that we do not harm our patients, waste public money, and achieve nothing.—I am, etc.,

Whitefield, Lancs. RONALD SAVIDGE.

Whither Natural Childbirth?

SIR,—I read with interest the recent letter by Dr. Constance Beynon, "Whither Natural Childbirth?" (*Journal*, February 19, p. 475). I disagree with the writer from the viewpoint of a midwife and that of the mother of two children. As a midwife I witnessed mothers in labour who had, as the writer says, "rehearsed" for it, and those who had a vague and sometimes no idea of what was about to happen. In the first cases fear was banished, which is a big step towards success; the use of drugs was reduced to a minimum, and complications to mother and baby were fewer. Sedation is used to help the mother relax, but often, owing to the use of drugs, the mother is unable to give of her best in the second stage, thus prolonging this stage. Asphyxiated babies are born due to over-sedation or sedation given at the wrong time. Instructions given to women in labour are of little or no avail.

Now from the viewpoint of a mother, which is the most important argument? I practised relaxation for each confinement. Pethidine and gas and air were given towards the end of the first stage when I had my first baby; due to this I neither appreciated what went on during the second stage nor did I help as much as I could have done. I certainly appreciated the use of pethidine and gas and air at that time, and wondered however I should get on without them when I was told when expecting my second baby that I could easily do without. They were certainly available if needed. When I went into labour I tried to relax as I had been taught, but did not achieve 100% success until the arrival of the person who had done the relaxation exercises with me during my pregnancy. I experienced no pain during contractions until the end of the first stage, and then only acute discomfort at the transitory period. The second stage was shorter because I had more energy to help, and I was brighter and more alert after the birth. If the physiotherapist, or whoever teaches the relaxation exercises, could be with the mothers in labour, or if midwives had a course in this art, then painless childbirth would be enjoyed by the many and not the few. Surely the money saved in drugs could be used to foster relaxation exercise clinics, and I am sure midwives would enjoy their work a lot more.—I am, etc.,

London, N.W.5. HONOR KENNY.

SIR,—I am glad that the subject of natural childbirth is being ventilated in the *Journal*. I agree with Dr. Grantly Dick Read (*Journal*, March 5, p. 604) that "childbirth is a much wider subject than obstetrics" and I welcome his plea for a "full inquiry into the care of pregnant and parturient women." Dr. Constance L. Beynon says (*Journal*, February

19, p. 475) that any other generation would think it absurd that child-bearing requires special training to be natural. But what pitiful stories one hears of child-bearing in the last two generations.

I am not in practice, but I talk to a number of women in my work for the Marriage Guidance Council, and I am impressed with how often difficulties in their own marriage relationship and the functions connected with child-bearing can be traced to the stories they have heard from their mothers, or to previous unhappy experiences of their own. I am also impressed by the eagerness of the young couples to whom I talk, either before or just after marriage, to know about these natural processes and the way this knowledge leads a young wife to the fulfilling experience of labour and motherhood.

I agree that partial knowledge or understanding may sometimes be dangerous, but only if a woman is allowed to go through labour unattended or without instruction at that time. The teaching of the antenatal clinic needs to be implemented in the labour ward; only so shall we enable a woman in labour to use, in the most helpful way, her spontaneous instincts of expulsion.—I am, etc.,

East Croydon. O. CYNTHIA HARRIS.

Gases in Artificial Respiration

SIR,—May I be allowed to discuss the comments of Dr. K. W. Donald and Professor W. D. M. Paton (*Journal*, March 12, p. 664) on my letter? I asked them for more evidence in support of their recommendation that oxygen with 7% carbon dioxide should be abandoned in the treatment of carbon monoxide poisoning. The only additional evidence they put forward is a paper by Schwerma *et al.*,[1] from which they quote the concluding sentence. Anyone interested should read the paper itself before accepting this quotation as having weight in settling the question of oxygen alone versus oxygen and carbon dioxide in the first-aid treatment of carbon monoxide poisoning. The reader will find: (1) The dogs who were given pure oxygen or carbon dioxide and oxygen had their respirations maintained by mechanical resuscitators. Mechanical respiration operates to weight the comparison in favour of oxygen and such respirators would not be likely to be available for first aid. (2) Here I quote the words and italics of Schwerma *et al.*: "It was impossible to keep the resuscitator mask on the dogs after they became conscious. *Our clearance studies are therefore based on the effect of a few minutes—usually two to four—of treatment followed by a period of four hours during which the animal was allowed to inhale air.*" Such brief administration was hopelessly inadequate.

To accord this paper the relevance and importance suggested by Dr. Donald and Professor Paton seems very strange. Even under the peculiar comparative conditions of their experiments, so unpractical when related to human first aid, the findings of Schwerma *et al.*, as recorded in their graph, showed clearance of carbon monoxide from the blood from almost lethal levels (over 80%) to levels compatible with life to be twice as fast—twenty minutes as compared with forty minutes to fall to 45%—in ten dogs who received 7% carbon dioxide and 93% oxygen (without rebreathing) compared with ten dogs who received 100% oxygen. If the time of administration had been adequate and mechanical resuscitators not used (the conditions of first aid to human beings), clearance from dangerous levels would probably have been about four times as fast for carbon dioxide and oxygen compared with pure oxygen.[2] This paper of Schwerma *et al.*, plus two slight papers, written 30 years ago, seems to be all the evidence, directly relating to carbon monoxide poisoning, that Dr. Donald and Professor Paton have to offer. They have not recorded any work of their own on carbon monoxide poisoning or attempted a balanced survey of the literature in which there are many more publications favourable to the use of carbon dioxide and oxygen than against.

In the first paragraph of their comments they defend their attitude by saying they were concerned with the full range of asphyxial emergencies and that correct diagnosis may not be within the power of the first-aid worker. The implication is that, if oxygen with 7% carbon dioxide is available to first-aid workers for the treatment of carbon monoxide poisoning, it may be wrongly used for patients with other forms of asphyxia in which there may be carbon-dioxide retention. This objection is hypothetical and not real. The first-aiders concerned are not usually presented with any diagnostic difficulty. There is not much doubt, to worry firemen, mine rescue workers, and ambulance men, about what is wrong with asphyxiated persons removed from burning buildings or gas-filled mines or rooms. Such first-aid workers are trained individuals and they can be told, if it is thought advisable, only to use oxygen and carbon dioxide for poisoning by carbon monoxide.

The most serious aspect of the whole matter is that apparently the Medical Research Council Committee is issuing, or has issued, a memorandum or directive advising cessation of the use of oxygen and carbon dioxide in the treatment of carbon monoxide poisoning—a reversion to the position of the early 1920's. Such a memorandum, coming from the Medical Research Council, will be regarded as authoritative and made the basis of administrative orders regarding the first-aid equipment of the rescue services. If it so happens that the advice is wrong, then many lives will be lost that might have been saved. Experimental re-investigation on animals and human volunteers could be easily and quickly done by use of the resources of the Medical Research Council. With great respect, I submit that it is the responsibility and duty of this Committee to sponsor such work if it is giving *official* guidance *which is contrary to generally accepted opinion.*—I am, etc.,

London, W.1. H. L. MARRIOTT.

REFERENCES

1 Schwerma, H., *et al.*, *J. appl. Physiol.*, 1948, **1**, 350.
2 Henderson, Y., and Haggard, H. W., *Noxious Gases*, 1943, 2nd ed., p. 285. Reinhold Publishing Corporation, New York.

Mental Confusion after Porto-caval Anastomosis

SIR,—The article by Drs. L. J. Hurwitz and R. S. Allison on recurring mental confusion after porto-caval anastomosis (*Journal*, February 12, p. 387) prompts me to report a similar case which recently came under my notice through the courtesy of Professor F. A. R. Stammers.

The patient was a woman, aged 60, admitted to the Queen Elizabeth Hospital, Birmingham, under his care on June 5, 1954. Two years earlier she had had a haematemesis, and in September, 1953, it was discovered that her spleen was enlarged and that oesophageal varices were visible with a barium swallow. Two weeks before admission she again had a haematemesis, followed a few days later by another. At the time of her admission she was greatly exsanguinated (R.B.C.s 1.82 m., Hb 3.9 g.) and occult blood tests were strongly positive. There were prominent veins on the abdominal wall, and the liver and spleen were both enlarged. Other systems were healthy. Pulse 80 per minute, B.P. 140/65. Liver function tests were abnormal (total serum protein 6.2 g.%, A:G 1.6:1; $ZnSO_4$ turbidity 5.0 units, $ZnSO_4$ flocculation +++; thymol turbidity 3.0 units, thymol flocculation +; colloidal gold Patterson 3, Maclagan ++++; serum bilirubin 0.5 mg.%; total cholesterol 145 mg.%; serum alkaline phosphatase 17.1 units%) and a splenogram showed typical intrahepatic portal obstruction. After multiple transfusions Professor Stammers carried out porto-caval anastomosis on June 26, 1954. Post-operatively all went well until July 13, when she suddenly became rather confused and disorientated, but in the course of a few days her mental state improved sufficiently for her to be sent out of hospital on July 22 to convalesce at her sister's home.

However, at her sister's her behaviour became so strange that she was admitted on a temporary order to a mental hospital, from which she was transferred once more to Professor Stammers at the Queen Elizabeth Hospital on August 13. I saw her on August 19, and made the following note: "She is very confused and forgetful, and cannot perform any difficult tasks to order, because she loses the thread of what she is meant to be doing too quickly. She calculated the cost of six 2½d. stamps very fast, and is good with multiplication tables, but more complicated mental arithmetic is quite beyond her—for example, the cost of four gallons of petrol at 4s. 6½d. a gallon. She has no trouble naming her own left or right sides, or her fingers, although she is easily puzzled about the examiner's. Given her dressing-gown to put on, she got into it back to front three times in succession, each time confabulating excuses for its not buttoning up in front. Asked about herself, she says she has been 'a little nervous' since the operation, but that it is 'nothing unexpected' in a person of her age. On physical examination there

is a rhythmic tremor of the head, and a regular alternating postural tremor of the hands appears from time to time (it was most noticeable when she was holding a pencil, and appeared plainly in her handwriting). No definite tremor of legs seen. There is occasional cogwheel snatch to be felt in the wrist and elbow on right, not so distinct on left, and none in legs. The deep reflexes are normal and the plantars flexor. There is a well-marked arcus senilis bilaterally and possibly some pigmentation on the limbic side of this, ? Kayser-Fleischer ring."

Liver function tests were then repeated, and gave results now distinctly more abnormal than before operation (total serum protein 6.8 g.%, A:G 0.94:1, $ZnSO_4$ turbidity 10.0 units, $ZnSO_4$ flocculation +++; thymol turbidity 5.0 units, thymol flocculation ++++; colloidal gold Patterson 5, Maclagan +++; serum bilirubin 1.5 mg.%; total cholesterol 220 mg.%; serum alkaline phosphatase 20.4 units%). The urinary amino-acid chromatogram showed normal excretion (traces of cysteine, serine, glycine, glutamine, alanine, and valine), and estimation of serum and urinary copper levels also gave results within the normal range (118 μg.% and 33 μg. per 24 hours respectively). Slit-lamp examination did not confirm the suspicion of a Kayser-Fleischer ring. The E.E.G. record was grossly and diffusely abnormal and showed persistent medium and high voltage slow activity at 2.5–5 c/s in all leads, and intermittent phase reversal was seen at both temporal electrodes.

It was clear that the cerebral condition must be of hepatogenous origin, and presumably of the same general nature as that which causes liver coma. From the neurological point of view the interesting points were the tremor of head and hands, which was typically extrapyramidal in appearance, the apraxia over dressing and difficulty in calculating, reminiscent of Gerstmann's syndrome of the parieto-temporal confluence, and the tendency to confabulate explanations of her difficulties. Her E.E.G. abnormality was of the type frequently seen in confusional states arising from a variety of causes, amongst them hepatic coma. The patient was discharged from hospital to her own home a few days after I saw her, and I understand that she subsequently made good progress.—I am, etc.,

Birmingham, 15. MICHAEL JEFFERSON.

Changes in the Mental Health Services

SIR,—Dr. F. Pilkington (*Journal*, January 29, p. 291) states that there is no clear definition of what constitutes a "mental observation ward." But surely he was arguing against the analysis which he himself submitted—that is, a total of 146 persons admitted under 3- and 14-day order (with no waiting-list or hindrance) and the liberty of the subject safeguarded by judicial authority. Of these, 107 became voluntary. Such transition should be easy and helpful to all concerned. Hence the ward is a "detention ward," vitally necessary for persons who, whilst mentally unbalanced temporarily, may injure themselves or others.

I know of many persons who have been grateful for enforced removal, thus being saved from the results of temporary mental aberration. Sometimes even the shock of a person being removed from his home has the effect of helping to bring him to his senses before the expiration of 3 or 14 days. Then a magistrate can, with doctor's help, discharge the patient to his home, and thus a bed is saved at the mental hospital for psychotic patients. Most mental hospitals are long distances from populated centres, and transport by ambulance over this distance is uneconomical.

Regarding the allegation of an undesirable change of doctor, I suggest that the consultant psychiatrist and his assistants (who are probably attached to the mental hospital) would see these patients anyway, and there would be no change of doctor. In my opinion, the Royal Commission should recommend that "detention wards" known as "observation wards" be instituted and designated in all well-populated areas for the urgent immediate care of the mentally sick, other than voluntary patients, and for the essential help and safeguard needed by the harassed G.P.—I am, etc.,

Plymouth. A. S. BRADLAW.

Defects of Modern Treatment of Leprosy

SIR,—I have read with interest the report (*Journal*, March 5, p. 597) of the meeting of the Edinburgh Branch of the Royal Society of Tropical Medicine on March 2, at which my friend, Dr. James Ross Innes, spoke on the above subject. With most of what he is reported as saying no one would disagree; he is obviously stressing the important point that modern treatment of leprosy, although a great step forward, has not solved the leprosy problem, and that further research is urgently needed.

I think, however, he rather misstates his case when he says that "the modern treatment of leprosy based on the sulphone group of drugs is unsatisfactory," for the reason that their slowness and imperfection of action suggested that it might prove very hard to eradicate the hard core of endemic infection. Surely a similar statement could be made of the modern treatment of almost any chronic infectious disease, with the possible exception of yaws. This does not appear an adequate reason for labelling a treatment as unsatisfactory.

Regarding the value of sulphone treatment of leprosy in the control of the disease in a community, we can as yet say little because of lack of evidence. Some workers think that with a disease such as leprosy, which usually propagates itself with so much difficulty, and even dies out spontaneously under certain circumstances, sulphone treatment, with all its limitations, may, by reducing the already low degree of infectivity, exert a definite influence in producing a decline of the disease. Other workers, including Dr. Ross Innes, think that before this result is obtained a more potent therapeutic agent is necessary. All workers, however, are keen to find more potent drugs, and trials of new drugs are constantly being made. All are keen, if possible, to apply immunization methods in the control of leprosy, and the possible value of B.C.G. vaccination for this purpose is being studied. It is good that these two lines of study are to be pursued by the research unit of which Dr. Ross Innes is in charge, which, by the way, this association has been instrumental in establishing.—I am, etc.,

London, W.1. JOHN LOWE,
Medical Secretary, The British Empire Leprosy Relief Association.

A Foreign Body in the Kidney

SIR,—Sir Heneage Ogilvie (*Journal*, February 5, p. 352), referring to a case reported by Dr. Duncan Macaulay and Mr. Thomas Moore (*Journal*, January 22, p. 205), describes a "kirbigrip" as "a small, smooth object, chemically harmless, without projections or points, ideally shaped to go round intestinal curves." Whether this is, or is not, an accurate description depends, as the late Professor Joad would have said, upon what one means by small and points. It is surely the length of a kirbigrip (4.8 cm. in Macaulay and Moore's case) relative to the lumen of the duodenum and the angle of the U-shaped curve of the second part of the duodenum that has to be considered. Though the ends are not sharpened, they are certainly pointed, and their slightly splayed arrangement probably makes it easy for the kirbigrip to impact in the duodenal mucosa. We are not told the age of the patient who swallowed the 6-in. (15.2-cm.) nail. I am, however, wholeheartedly in agreement that of all ingested foreign bodies the kirbigrip has the most evil reputation.

Several times a year one faces the problem of a kirbigrip in the stomach or already in the duodenum of a child, the parents clamouring for instant removal, or alternatively refusing consent for operation if there is a chance that the kirbigrip will pass spontaneously. Sometimes the parents have already been told by their doctor that the foreign body should be removed at once or that it will certainly pass. I believe there is something to be said for removal of a kirbigrip from the stomach of a child of less than 2½ years of age. The operation is almost foolproof, and saves much anxiety and frequent radiological examinations. When the

kirbigrip is in the duodenum, and especially if it remains in the same position, as shown by daily films, it is probably wise to remove it after 2–3 weeks. In my experience a kirbigrip which negotiates the U-shaped bend usually passes without incident. I have only seen three instances of delay at the duodeno-jejunal junction; two were removed after 2–3 weeks' observation and the third passed onwards after two weeks. I have not seen perforation of the bowel at this site.

I have had one child in which the hair-slide was partly in the kidney and partly in the duodenum at the time of operation—there were no urinary symptoms—and one which presented with a limp in which the kirbigrip was removed from the psoas muscle. Both perforated "pointed" end forward; in the second case, by the time the kirbigrip was removed it was in two pieces, the loop end having corroded away. I have probably removed upwards of a dozen kirbigrips from the duodenum after waiting up to three weeks. With good anaesthesia, an adequate incision, and closure of the duodenum with non-absorbable material, the operation is easy and safe.—I am, etc.,

Liverpool. ISABELLA FORSHALL.

Dyspareunia

SIR,—I was most interested to read that Mr. R. Christie Brown (*Journal*, January 8, p. 106) is starting a clinic to study dyspareunia as a cause of sterility. Here in Uganda we have a tremendously high incidence of sterility, but one hardly ever meets the type of dyspareunia that is seen in the United Kingdom. If difficulty or pain on intercourse is experienced, there is in practically every case a true organic cause—in fact one wonders why it is not a much commoner symptom. Out of 1,035 patients who thought their condition sufficiently serious to come into the gynaecological wards at Mulago Hospital last year, only six complained of dyspareunia. In four of these the cause was only too obvious. Two had a large pyosalpinx, one a badly stenosed vagina following trauma at childbirth, whilst another was an interesting case of a Nubian woman from the Sudan who had undergone female circumcision as a child and, on marriage, discovered that the entrance to the vagina was almost completely occluded. This is a rare complication of circumcision in the female. The other two patients were certainly a little more of the type found at home. A woman of 30 years of age, married about eight years, had an unruptured hymen and complained of dyspareunia. However, she also had uterine fibroids, which seemed to worry her even more. In one case only there was no apparent cause, an examination under anaesthetic revealing nothing abnormal.

Dr. G. W. Theobald states in his letter (*Journal*, January 22, p. 228) that cauterizing the cervix may help to cure some cases—presumably working on the theory that chronic cervical infection causes many gynaecological symptoms. Here we have a superabundance of chronic cervicitis, practically all of gonococcal origin, but only rarely is backache or dyspareunia found. Some do complain of lower abdominal pain, however. It does appear that the complexities and anxieties of civilized life cause many marital difficulties. Here, coitus, childbirth, and breast-feeding are all accepted as perfectly natural functions, and, unless there is something organically wrong, no particular trouble is experienced by the African woman.—I am, etc.,

Kampala, Uganda. CORALIE RENDLE-SHORT.

Tonsillectomy

SIR,—As an anaesthetist, it is with some trepidation that I enter the tonsil controversy, but, since Dr. H. B. C. Sandiford (*Journal*, March 5, p. 603) has cited anaesthesia as an important factor, I feel justified in joining the fray.

The only advantage of the guillotine operation is presumably that you can do "more than ten rather than less than four per hour." Dr. Sandiford quotes two satisfactory anaesthetic techniques; the first of these, $N_2O \rightarrow O_2 \rightarrow$ether with oral or nasal intubation, would have to be carried to at least the second, preferably the third, plane of surgical anaesthesia to produce the ideal operating conditions which Dr. Sandiford so rightly demands. I doubt the ability of many anaesthetists, working single-handed, to anaesthetize more than ten cases in this manner inside an hour, let alone for the surgeon also to operate on them—without a two-minute time limit. Also, the statement that turning off the ether when the gag is inserted "ensures that the patient will be in a light plane of anaesthesia at the end of the operation *regardless of time*" (my italics) is somewhat extraordinary; if the patient is deep enough to tolerate gag, tube, and operation lasting two or three minutes, it is difficult to see by what mechanism he is "in a light plane of anaesthesia" at the end of it; it is, of course, almost completely dependent upon "time." The better the operating conditions and the better the operator, the deeper will be the patient at the finish, whichever way the knobs are turned in the meanwhile.

With regard to the second anaesthetic technique—namely, a single injection of thiopentone only—I can only say that if this technique should become widespread my own children will hang on to their tonsils until they are so bad that even the most enthusiastic guillotinist would not consider them suitable for this type of operation or "anaesthetic," and the inverted commas are intentional.—I am, etc.,

London, W.14. M. P. COPLANS.

SIR,—I have read with interest Dr. J. B. Stirling's comments (*Journal*, February 26, p. 542). The advantages of the technique I advocated (*Journal*, January 29, p. 285) over that used by Dr. Stirling are that an injection of atropine, with its adverse effects on psyche and soma, is avoided, and that with efficient team-work and the use of a recovery room 16 to 20 cases can comfortably be done in an hour. Relaxation is adequate for opening the jaws and for a clean guillotine tonsillectomy, and tachypnoea does not occur.—I am, etc.,

Hull. W. N. ROLLASON.

Intramuscular Iron

SIR,—The widespread interest aroused by the introduction of an iron dextran complex ("imferon") for intramuscular administration is evident from the volume of correspondence which has appeared in the *Journal*. There would seem, however, to be some difference of opinion regarding the value of, and indeed the necessity for, such a preparation. It has even been suggested that oral administration of iron is the only method which need be used. We should like to make known our views on imferon, and to stress certain aspects of its use and of the technique of administration.

We first began to use this complex over thirteen months ago when we carried out some of the earliest clinical trials. It was initially given to 30 patients who were selected after full haematological investigation and shown to suffer from iron deficiency; some of them were cases of primary hypochromic anaemia (Witts's anaemia); others were associated with dietetic deficiency occasioned by such conditions as peptic ulcer (even where no frank or occult bleeding occurred), or by financial difficulty in elderly people living alone. Many had been given oral iron in apparently adequate dosage without appreciable effect, while a number had admittedly not been taking the iron prescribed by their doctors. We did not include patients suffering from such conditions as advancing malignant disease or chronic nephritis. All patients underwent bone marrow studies and fractional gastric analysis, and possible causes of chronic blood loss were sought for and excluded. Our conclusions were as follows: (1) Imferon is readily absorbed and produces a completely satisfactory haematological response. (2) It is non-toxic both locally and generally when administered in the correct dosage, and when reasonable care is taken in selecting the site of injection and the type of case to which it is given. (3) Its administration can safely be entrusted to any competent nurse.

We should like to emphasize the importance of ensuring that the substance is deposited in the muscle and not in the subcutaneous fat. If this is not done, then marked staining of the skin

will certainly occur, and, while we have not encountered any serious trouble in this direction, patients are apt to object to the cosmetic effect.

Since the original series was studied we have used imferon on a large number of other patients, and have had no cause to change our opinion that it represents a distinct advance in iron therapy. Its advantages over intravenous preparations are so obvious as to require no further comment. Imferon itself has been given intravenously, but some side-effects have been reported, and there seems to be no valid reason for administering in this way a substance which was expressly produced to avoid the hazards of such therapy.—I am, etc.,

A. GRUNBERG.
J. L. BLAIR.

Birkenhead.

Silver Stool Sign

SIR,—Sir Heneage Ogilvie's memorandum on "Thomas's Sign or the Silver Stool in Carcinoma of the Ampulla of Vater" (*Journal*, January 22, p. 208) appears to have evoked considerable correspondence. The following case may consequently be of interest.

A male patient aged 71 years was admitted on February 10 with a ten-day history of painless jaundice of increasing intensity following upon an attack of bronchopneumonia. The patient died from cholaemia 17 hours after admission, but before death passed a stool of unusual appearance, which was kept by the night staff for me to see. To my surprise this stool was the colour of aluminium paint, and, having read of the diagnostic import of Thomas's sign, I consequently made a confident post-mortem diagnosis of hepatic failure following upon carcinoma of the ampulla of Vater. To my disappointment necropsy revealed a carcinoma of the gall-bladder, with metastatic deposits around the porta hepatis and quite normal ampulla of Vater.—I am, etc.,

Gravesend, Kent. C. A. M. WALKLEY.

SIR,—In my memorandum (*Journal*, January 22, p. 208) I did not make it sufficiently clear that the Thomas stool has the grey colour of oxidized silver or aluminium paint rather than the sheen of a new half-crown. Fatty acid crystals appear in the faeces in various disorders of fat metabolism and give the stool that metallic lustre to which your correspondents have drawn attention, but the appearance is that of brass filings rather than of silver. The classical Thomas stool is due to the mixture of blood (black) with fat (white) and it is rarely seen except in cancer of the ampulla.—I am, etc.,

London, N.W.8. HENEAGE OGILVIE.

Grants for New Hospitals

SIR,—I disagree with Mr. R. S. Murley's objection (*Journal*, March 5, p. 600) to the building of new hospitals, and with his preference for the improvements that may be possible in old and unsuitable buildings. It is very encouraging that regional boards are to have control of new hospitals. In order to produce the greatest effect of this encouragement it is hoped that the Minister of Health will announce the aim to provide patients in every part of the country with medical facilities and with amenities of a modern standard. This will need a more equal expenditure than at present on all hospitals—teaching and non-teaching; regional boards owe it to the patients in *their* hospitals to press unceasingly for this.—I am, etc.,

London, W.1. J. M. ALSTON.

Fluoridation of Public Water Supplies

SIR,—We are gratified that the members of the U.K. Mission on Fluoridation (*Journal*, March 12, p. 667) share our desire for more knowledge (*Journal*, January 29, p. 284); the need for this was the main stimulus of our letter. We note they believe the strongest evidence against dietary fluoride having any deleterious effect comes from the study of two areas in Texas; the validity of the statistics from these areas has already been questioned (*Journal*, February 26, p. 538).

The members of the mission regard as misleading our statement that the effect on dental caries in adults of the ingestion of water containing 1 p.p.m. is much less certain than the well-established effect in children up to the age of about 8 years. Yet a member of the mission himself stated (*Journal*, January 22, p. 224) that one of the four main conclusions of the mission was that there is abundant evidence that lifelong consumption of such water "results in a substantial reduction of the incidence of dental caries in children, and probably in adults also." If there is this doubt about adults who have consumed such water from birth, we still feel justified in believing the effect upon caries in adults partaking of it after childhood to be "much less certain" than the "well-established" effect in children.

If we interpret the members of the mission correctly, they suggest the "severe dental fluorosis" found by one of us (D. C. W.) in Oxfordshire might have been caused by the hypoplasia due to exanthematous diseases or nutritional disturbances during enamel development. The original publication[1] included a photograph of teeth which do not seem to us or to those whom we have consulted to resemble changes that could arise from either of these two conditions; more important, the publication mentions that Dr. Ainsworth, to whom we are all indebted for the classic description of teeth at Maldon,[2] himself visited one of the Oxfordshire villages and verified the findings.

We doubted the statement of the mission in their report that "in theory any fluorine compound which will ionize in aqueous solution should have the same action on teeth." The mission now appear to agree that their statement was not true, but they claim that, even if we were correct, our objection would not be a valid one, since no one, they allege, is proposing to use stannous fluoride. Fortunately, chemical theory is not altered by what anyone proposes to add to public water supplies.

Finally, we are surprised to learn from the members of the mission that fluoridation of water supplies would not be carried out in the neighbourhood where fluoride dust might settle. The horticultural industry uses such dusts, as is implied in a statement the mission quotes in its report (p. 57): "Fruits and vegetables may be contaminated with residual fluoride dusts following the use of fluoride-containing insecticides in orchards and fields." There may be further difficulty in implementing this assurance, since there are at least 28 known sources of atmospheric contamination by fluorides. And there would remain the problem of industries other than the horticultural industry that might be introduced later into an area that was already using fluoridated water; of such the recent outbreaks of animal fluorosis on lands which had been altered by opencast coal-mining are a reminder.[3]—We are, etc.,

H. M. SINCLAIR.
Oxford. DAGMAR C. WILSON.

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2 Ainsworth, N. J., *Brit. dent. J.*, 1933, **55**, 233.
3 Towers, K. G., *Vet. Rec.*, 1954, **66**, 355.

SIR,—I was interested to read the report of the Board of Faculty of Dental Surgery of the Royal College of Surgeons of England on the fluoridation of domestic water supplies (*Journal*, February 26, p. 535). When studying the incidence of dental fluorosis in certain districts in India, Dr. D. C. Wilson[1] noted that when dental fluorosis was present so also was goitre. In England geological formations containing fluorine are found in certain districts. One of these is Derbyshire, where it appears as fluorspar, and where it is, or until recently was, mined. At one time goitre was very prevalent in certain parts of this county; it is now much less common, probably as a result of improved water supplies. Rocks containing fluorine are found in other districts in England, and these districts are places where goitre is more or less prevalent. On her return to England Dr. Wilson

continued her investigations, and obtained additional evidence that fluorine in drinking-water may be a factor in the causation of endemic goitre.

Two points suggest themselves to me for consideration. First, how is the amount to be kept approximately at the fluorine dilution decided upon, and, secondly, would an action for damages lie against those responsible for the addition of fluorine to the water supply by one who developed goitre or the disfigurement of dental mottling?—I am, etc.,

Watford. THOMAS FENTEM.

REFERENCE

[1] *Lancet*, 1941, 1, 211.

Hexamethonium Ileus

SIR,—The memorandum by Dr. H. J. Goldsmith (*Journal*, February 26, p. 522) draws attention again to the dangerous complication of ileus which may arise from parenteral or, more commonly, oral dosage of hexamethonium, which has been commented upon previously. The large dosage of hexamethonium used in the case cited is attended by severe risk of inhibition of gastro-intestinal activity, owing to the generalized ganglionic blockade produced by this drug. Constipation and diarrhoea constitute an indication for immediate withdrawal of dosage.

Four cases of ileus were encountered when hexamethonium was first applied in the Royal Alexandra Infirmary, Paisley. Subsequently an investigation of methonium homologues[1] showed that pentolinium has much less effect upon the bowel than upon the blood pressure. This ganglion-blocking agent has been used since without producing ileus even during sustained oral dosage, although constipation has occurred infrequently. As Smirk *et al.* have shown,[2] the combination of pentolinium and reserpine is very useful in the treatment of patients with severe hypertension, and these drugs have almost entirely replaced hexamethonium in the treatment of hypertension in this hospital.—I am, etc.,

Paisley. J. GIBSON GRAHAM.

REFERENCES

[1] Maxwell, R. D. H., and Campbell, A. J. M., *Lancet*, 1953, 1, 455.
[2] Ibid., 1954, 2, 159.

Manipulation and Low Back Pain

SIR,—In our recent letter (*Journal*, January 29, p. 288) we suggested that Cyriax or his colleagues should produce figures to back up his claims of almost total success with manipulation in the treatment of disk lesions of the cervical, dorsal, and lumbar regions. In the *Journal* of March 19 (p. 705) two of his colleagues have published some results of manipulative treatment in that syndrome which can be described as "lumbago."

Drs. Anthony B. Coyer and Ian H. M. Curwen have treated a series of 152 patients by carrying out manipulations, or advising rest in bed with analgesics, to alternate patients. Comparison of the figures of these apparently contradictory methods of treatment shows several differences. The first is that 50% of the manipulated patients and only 20% of the others recovered during the first week. The second is that 28% of those rested had persisting symptoms after six weeks as compared with only 12% of those manipulated. There is a third difference in that 16 (21%) of the rested cases "did not carry out instructions, or did not report for assessment"; and these 16 are omitted from the results group in 2. Every one of the 16 was of working age (Table I), and it is important to know whether they had recovered spontaneously and returned to work in a week or so, or had sought treatment elsewhere and remained uncured. If they had in fact recovered within a week, the first outstanding difference in Coyer and Curwen's results would disappear, and we should then find from Table VI that, whether manipulated or not, about 50% of all the patients had recovered in a week, and about 30% after a further two weeks. That about 80% of patients suffering from an attack of "lumbago" will recover from that attack more or less spontaneously within about three weeks is a piece of information which, probably, most of the readers of this *Journal* would confirm from their own clinical or even personal experience. However, like most orthopaedic surgeons, we have found that quite a few cases of acute low back pain with fixation (lumbago) can be relieved immediately by a single manipulation without anaesthesia, if seen early enough and especially within a few hours of onset of the attack.

With regard to the second outstanding difference, is it possible that chance can have placed, in the whole of Group II, an uneven proportion of cases more difficult to deal with? We feel that this may be so because, comparing the two, in the second group there were 9% more patients over 30 years of age (Table I); 20% more had significant radiological changes (Table V: disk lesions, osteophytosis, osteoarthritic changes, etc.); and 12% more were using a sagging bed so perhaps went home to rest in those same beds (Table IV).—We are, etc.,

London, N.W.1. W. D. COLTART.
H. OSMOND-CLARKE.

Incubation Period of Herpes Zoster

SIR,—The incubation period of herpes zoster does not appear to be definitely established. The following case seems to point to an interval of two weeks from exposure to appearance of rash.

The patient, a woman of 50, had been indoors for six weeks and had had no visitors when she visited her hairdresser on February 9. The hairdresser had been in contact with his mother, whom I had attended for herpes zoster. My patient complained of severe lumbar pain on February 16, a week later. On February 23 the typical rash appeared in distribution L.2. Apart from her own family, the only outside contact had been her visit to the hairdresser, a fortnight before the appearance of the rash.—I am, etc.,

London, N.W.10. H. BROSTOFF.

Clinical Staging of Carcinoma of the Breast

SIR,—Those who work among cancer patients are becoming increasingly aware of the difficulties of comparing the results of treatment methods owing to the lack of agreement about staging this disease. The cervix uteri is the only site for which an international staging exists, and it is a reproach to cancer specialists all over the world that in the last 25 years there has, until recently, been no real effort to do the same for other sites. At the sixth congress of the Union Internationale Contre le Cancer held in Brazil in July, 1954, the staging of carcinoma in several sites was discussed—for example, the breast, larynx, and pharynx. Oddly enough, the staging of cancer of the larynx, which is a rare disease and which is treated on a large scale in comparatively few centres, provoked long and even acrimonious discussion. By contrast, breast staging was the subject of a number of proposals, but these aroused little interest and scarcely any debate.

It seems to many of my colleagues at the Royal Marsden Hospital (formerly the Royal Cancer Hospital) that international agreement on the staging of breast cancer is more urgently required than for any other site in the body, and this for the following reasons: (1) the high incidence of the disease; (2) the large number of clinicians treating the disease; (3) to discover the effect of any one treatment upon the disease so that different methods of treatment can be compared; (4) because the comparatively high survival rate would surely make this comparison worth while; and (5) because there seems to be a reasonable hope of achieving earlier diagnosis in cancer of the breast by appropriate propaganda than in most other cancer sites and therefore it is important to try and find out whether such propaganda would succeed in improving the results of treatment.

No doubt the World Health Organization is the proper body to decide the matter, and only they can effectively advise the universal adoption of a staging which will inevitably dissatisfy many people. The next meeting of the International Union against Cancer is in London in 1958. Is it

too much to hope that before then British surgeons and radiotherapists may have met, discussed, and agreed upon a clinical staging for carcinoma of the breast so that clinicians of this country at least can put forward a basis for discussion which already commands firm support?

This letter is written in the hope of stimulating interest and action and to say that the Royal Marsden Hospital is willing to take the initiative in arranging such meetings of clinicians as would be necessary to determine this matter if no official body is likely to do so in the very near future.—I am, etc.,

London, S.W.3. MICHAEL HARMER.

Hypodermic Injection Technique

SIR,—I feel that Dr. L. P. Lockhart's letter (*Journal*, February 12, p. 415) about hypodermic injections should be loud-pedalled. The law of averages is pretty safe, but the exception could often prove a fatality, especially with some of our heterogeneous penicillin formulations. On these grounds alone I deplore the growing popularity of the "cartridge" syringe.—I am, etc.,

Wrexham. R. P. W. KUP.

Coarctation of the Aorta

SIR,—In view of the recent correspondence on this subject, the following case merits recording.

The patient was admitted to Westminster Hospital under the late Sir James Purves-Stewart. She was aged 45 and had been short of breath for 20 years, during which she had had seven pregnancies, including a pair of twins at the age of 34, after which her breathlessness became more severe. There were three miscarriages. On examination she was severely dyspnoeic, the heart was enlarged, and there was a loud systolic murmur at the apex. Tortuous arteries were palpable in the neck and posterior and lateral aspects of the thorax. Blood pressure in the arms was 170/110. E.C.G. showed abnormal notching of the ventricular complex. She died suddenly of cardiac failure. At necropsy the aorta was so constricted that a ¼-in. (3.2-mm.) probe could not be passed. The aorta beyond this point was reduced to ½ in. (12.7 mm.) in diameter, but the collateral circulation was greatly hypertrophied. The ductus arteriosus was reduced to a fibrous cord and the other viscera showed signs of chronic venous congestion.

The case came to my notice because of the specimen of heart and aorta in the pathological museum at Westminster Medical School.—I am, etc.,

London, S.W.1. A. D. MORGAN.

Doctors and the Press

SIR,—Surely Dr. R. W. Cockshut (*Journal*, March 19, p. 731), in insisting on a policy of no capitulation and no compromise with the Press, is a little unrealistic. It rather reminds one of America's one-time splendid isolation. As a practical point it is the duty of the B.M.A.'s Public Relations Department to try to keep on friendly terms with the Press. There have been times when we have been only too glad of their help. One does not remain friends by a glassy stare and a reiteration of "No comment!" The popular press is, by definition, popular. Dr. Cockshut may not like it, but most of his patients do, and they not only lap up with avidity the sort of material he objects to but in many cases would rejoice to see themselves, complete with their troubles, right on the front page. Still, he wishes to protect them against their worse selves.

The majority of journalists are highly responsible people, and, if we wish to get their co-operation in restraining their more ebullient colleagues, surely compromise and mutual understanding are essential. A surgeon is fully entitled to object to reporters invading his hospital. I imagine there would be an equal objection if a squad of doctors burst into an editorial conference of the *Daily Mirror* and wished to take the temperatures of all present. Such things are insufferable, but there are old and tried methods of coping with gate crashers, and we do not need special medical measures.

All doctors object to personal publicity, and the Press, plagued every day by publicity hunters, finds this difficult to understand. Only by friendliness can we make them understand—but remember that anything in print in the *Medical Directory* or in *Who's Who* is public property, legally and ethically quotable. All one can ask is for no fulsome additions. We must, of course, always shield our patients—provided they wish to be shielded. But, as I have said, quite a lot do not, and will treasure all their lives the copy of the paper with their deformed picture on the front page. If we withhold information, they give it—so do their friends and neighbours.

In short, this is not a simple problem of "mind your own damned business," but one which well deserves a most thoughtful conference.—I am, etc.,

Ashtead, Surrey. W. EDWARDS.

SIR,—Dr. R. W. Cockshut (*Journal*, March 19, p. 731) appears to be rather out of touch with the facts. For some time it has been the accepted custom for doctors of the highest ethical standing to publish news bulletins on the state of health of persons deemed of interest to the public. Dr. Cockshut's urging the medical representatives at the forthcoming conference with the Press "to present the view that the physical and mental misfortunes of our patients do not constitute legitimate 'news'" is, therefore, even further removed from reality than his statement that Professor Ian Aird recently wrote a letter to the *Observer* on this subject. It was, in fact, an interview.

The exploitation of human misery by the Press or, of course, by the medical profession is damnable. But I have an uneasy feeling that some of the indignation being felt over the plight of the person most concerned in the news story that first drew attention to this whole matter is misplaced. In the course of a lengthy interview with Mrs. Davies she told me that she read "all the papers, especially the picture ones." She liked what they said about her and the twins. She thought that all the reporters who had come to see her were "very nice," with two exceptions. These, by the way, were *not* free-lance journalists. As for the public's reaction to what appeared in the newspapers, she had found everyone sympathetic and kind. She seemed delighted with the presents, letters, messages of good will, and offers of prayers that came her way because of the Press. Seeing that Boko and Tomu were "news" it was a great pity, when Mrs. Davies's permission was forthcoming, that the distribution of news from the hospital was not more adroitly handled. Scanty news bulletins were issued through the press officer of the large business house which had a finger in the pie, but none of the 11 doctors involved in the preliminary investigations or the operation was available to answer the obvious questions, while the surgeon most mentioned in connexion with the case refused to answer the telephone.

The unhappy result of this policy was that reporters waiting outside the hospital on the day of the operation sought news from any available source. One of the doctors who had just left the theatre said that the operation had been a success and that "Professor —— had been wonderful." This news was rushed to afternoon papers which came out on the streets about the same time as the message from the hospital reached other parts of the hospital that one of the twins was dead.

The Press had another grievance. One national newspaper asked to use some of the pictures being taken during the operation. But the reply was that these pictures were intended for strictly medical or scientific scrutiny. Yet shortly afterwards some of these pictures were published by a weekly non-medical illustrated magazine. How did this leakage occur? And why was there no protest from the hospital at the time?

Over a year ago (*Journal*, January 16, 1954, p. 141) you mentioned the need for a clearer understanding by the medical profession and the Press of each other's problems and your hint has finally been taken. But on the same

occasion you suggested that if any surgeon were faced in the future with the dilemma that confronted Professor Aird over the Davies twins he would be well advised at the outset to seek the help of the public relations officer of the B.M.A., and thus make use of the facilities available in his own professional organization. According to a letter from your public relations officer, Mr. John Pringle, to *The Times*, this help was offered in connexion with the recent Siamese twins, but was refused. Now, Dr. Cockshut, commenting on Mr. Pringle's letter, says that it "seemed to impute that the surgeons concerned bore some responsibility through a failure to approach him or accept his offer of help." If the phrase means responsibility for what happened between the Press and the other interested parties, then I am in hearty agreement with your official in his belief that if the B.M.A. public relations officer had been invited to intervene between the doctors and the Press much of the ensuing unpleasantness could have been avoided.

In this I believe I am voicing the views of many of my colleagues in journalism. The B.M.A. "Press office" is the clearing-house for an immense amount of reliable medical information which is given promptly to the Press. That office promotes the best possible relations between the profession and the Press to the benefit of both. I feel confident that if the help of the B.M.A. had been accepted in the two cases under consideration Mr. Pringle and his staff would "have had the courteous co-operation of all but the least reputable elements of the Press."—I am, etc.,

ALFRED BYRNE,
Medical Correspondent, *Manchester Guardian*.

London, E.C.4.

The Discovery of Penicillin

SIR,—To your excellent leading article "The Discovery of Penicillin" (*Journal*, March 19, p. 711), in which you quote from Alexander Fleming's first paper on penicillin, I would like to add two more paragraphs from two other of his papers: "It is quite likely that it [penicillin] or a chemical of a similar nature will be used in the treatment of septic wounds,"[1] and: "It [penicillin] has been used on a number of indolent septic wounds and has certainly appeared to be superior to dressings containing potent chemicals."[2]

It is marvellous to see how thoroughly Fleming carried out alone his remarkable work, and how he insisted, in three different publications in 1929, 1931, and 1932, on the possible therapeutic use of penicillin in the treatment of septic wounds infected with penicillin-sensitive microbes.—I am, etc.,

F. BUSTINZA.

Madrid.

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2 —— *J. Path. Bact.*, 1932, **35**, 831.

Relief for Medical Victims of New South Wales Flood Disaster

SIR,—I have ascertained that the New South Wales Branch of the Association is organizing a fund for the relief of the doctors who have suffered as a result of the recent floods which caused widespread devastation in that State. I am sure that many members of the Association at home will welcome an opportunity of making a small contribution to this fund, and that help of this kind from the profession in the mother country will be greatly appreciated by our Australian colleagues. I shall therefore be happy to receive donations for transmission to the New South Wales Branch in Sydney.

Will contributors please make their cheques or postal orders payable to "The British Medical Association" and send them to the Chairman of Council, B.M.A. House, Tavistock Square, London, W.C.1, marking the envelope "N.S.W. Relief Fund" in the top left-hand corner?—I am, etc.,

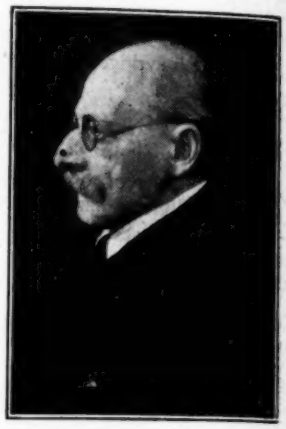
E. A. GREGG,
Chairman of Council.

London, W.C.1.

Obituary

MAX NEUBURGER, M.D., Ph.D.

Professor Max Neuburger, the great historian of medicine, died in his native Vienna on March 15 after a long illness. He was in his 87th year, and for over forty of these he had taught his subject in the University of Vienna. He had written or edited seventeen books and about 180 papers, had founded and equipped a famous institute largely without official help, and had received decorations from five countries and honorary fellowship or membership of many learned bodies.



Max Neuburger was born in Vienna on December 8, 1868. He was descended from Jewish families which had long been resident in Munich and Hamburg. His father, Ferdinand Neuburger, was a brilliant linguist; a native of Munich, he migrated to Vienna as a youth and became an Austrian subject in 1859. Max attended the Piaristengymnasium and then studied medicine at the University of Vienna, having among his teachers such famous men as Billroth, Nothnagel, Krafft-Ebing, Fuchs, and Politzer. Very important for his early career was Moritz Benedikt, who taught neurology. Neuburger graduated as a Doctor of Medicine in 1893, and he then spent two years as resident physician (*Secundararzt*) at the Rudolfspital. In 1896 he became assistant to Benedikt at the Allgemeine Poliklinik, a post which he held until 1908, and he became a well-known neurologist. Although he wrote little on the modern aspects of his subject, he influenced its development by his historical writings. He had a private neurological practice until 1914, but he voluntarily sacrificed more and more of this lucrative work for the sake of his humanistic studies. During the first world war he was in charge of several military hospitals, and the end of the war marked the close of his active clinical career.

For the following account of Professor Neuburger's work as a medical historian we are indebted to Dr. E. ASHWORTH UNDERWOOD: While he was still a student Neuburger published several short historical-philosophical articles. At this time the chair of the history of medicine was held by Theodor Puschmann, who had published his history of medical education in 1889. After his graduation in 1893 Neuburger was inspired and encouraged by Puschmann to carry out historical studies. Within the next two years he wrote several papers, one of which demonstrated the pioneer work of Giuseppe Zambeccari as an experimental physiologist. Puschmann now encouraged Neuburger to become a Dozent, and for this it was necessary for the candidate to submit a published thesis. The result was Neuburger's important work on the history of the experimental physiology of the brain and spinal cord to the time of Flourens (1897). In 1898 he was appointed as a Privatdozent—an honorary lecturer—and his real career had officially commenced. Thus started his long association with Robert Ritter von Töply, who was twelve years his senior. Von Töply was an active military surgeon who later rose in the Austrian Army to a rank corresponding to our Director-General of

Medical Services. He was a keen medical historian, and he also was appointed Privatdozent under Puschmann : a few years later he wrote the long section on anatomy in the famous *Handbuch der Geschichte der Medizin*. Puschmann died in 1899, and the teaching was carried on by the Dozents, von Töply and Neuburger. In 1904 Neuburger became extraordinary professor, and full professor in 1912. He retired officially in 1934, but continued the work until 1938.

Neuburger's work falls naturally into two parts—his writings and the foundation of the Vienna Institute for the History of Medicine. For his research work he was superbly equipped by nature, by training, and by experience. He was endowed with a consuming interest in the medicine of all ages and of all peoples, without which none can aspire to the title of general historian, and with a historical sense which is given to few. He was gifted with a literary style of great purity and dignity. To these assets he could add his sound basic training in many languages and in historical methods. He made few detailed studies of ancient texts, and his main interest was the synthesis of the history of a subject in relation to the various cultures of the periods discussed. He has been rightly called the most philosophical of the great historians of medicine.

Neuburger's first book, his *Habilitationsschrift* on the history of the experimental physiology of the brain and spinal cord, published in 1897, is a very learned discussion of this difficult subject from Willis to Flourens and Magendie. Two other monographs, on specific nutrition and on the early history of antitoxin therapy, followed quite soon. Puschmann had expressed the wish that the enormous *Handbuch* which he had planned was, in case of his death, to be edited by Neuburger, but when Puschmann died with his task scarcely begun the publisher requested Julius Pagel, of Berlin—it would seem quite rightly, in view of the size of the work—to act as co-editor with Neuburger. The first volume, dealing with the whole field up to the Middle Ages, appeared in 1902. The second and third volumes, dealing with the histories of individual subjects, were published in 1903 and 1905. Neuburger's long introduction to the second volume is evidence of the accuracy of his scholarship and the width of his interests ; in itself it would have been sufficient to establish him as a considerable historian. Of the other books which he later wrote, mention must be made of his definite biography of Hermann Nothnagel, and of his several major contributions to the history of the Viennese School. His long book on the doctrine of the *vis medicatrix naturae* (1926) in itself demonstrates the main characteristics of his work.

While he was labouring on the *Handbuch* Neuburger was also engaged on preparing his own *History of Medicine*. The first volume of this work was published in 1906, and carries the subject to the end of classical antiquity. The second volume—to the close of the Middle Ages—appeared in 1910. Neuburger never finished this great work. From a letter written late in life it is clear that he was preparing the Renaissance section in 1920. Under the sponsorship of Osler an English translation began to come out in 1910 and was completed in 1925. The history was not intended for the specialist. It is learned, very accurate, and puts each subject against the background of its time. Its only disadvantage is the intentional paucity of references.

Puschmann had intended to found an institute for the history of medicine at Vienna, but after his death the funds with which he intended to accomplish this were diverted to Leipzig. The new institute was founded there in 1905. It was endowed from the start and Sudhoff became its first director. In 1906 Neuburger and von Töply presented a memorandum to the Ministry of Education in Vienna, emphasizing the necessity for an institute, and explaining how its museum collection could be built up from material already in the possession of other institutes and hospitals. They launched a newspaper appeal for books, portraits, and museum objects. Von Töply soon retired from active participation, and the building up of the institute is due to Neuburger alone. He presented to it 1,000 books and reprints from his own library and worked unceasingly to expand the collections and to obtain rooms for them and his seminars. They were first housed in a small space below a lecture theatre. In 1919 Neuburger had them transferred to three rooms in the national building called the Josephinum. The medical library of the Josephinum and its magnificent collection of 1,200 wax anatomical models were added to the institute. By 1934 the institute was occupying 15 rooms. On his 60th birthday a volume of essays was issued in his honour, and his portrait-medal was struck in Vienna. In 1930 Fielding H. Garrison edited in his honour a volume of translations of twelve of Neuburger's studies.

In 1939 arrangements were made for Neuburger to join the scientific staff of the Wellcome Historical Medical Museum. He arrived in London on August 26, 1939, with two suitcases and five shillings. Kind friends looked after him in his new surroundings. During the war he underwent a serious operation, and he stuck doggedly in London throughout the bombing. Practically all his previous work had been written in German, but he now began to write and publish in English. His interests became more and more centred on British medicine, and in 1943 he published a charming little book entitled *British Medicine and the Vienna School : Contrasts and Parallels*. He continued to work steadily until June, 1948, when he departed for the United States to live with his son in Buffalo. Later that year another volume of essays in his honour, edited by Dr. Emanuel Berghoff, was published in Vienna. Dr. Berghoff's biography of Neuburger, in German, was published at the same time. During four somewhat restive years Neuburger tried to accustom himself to the American way of life, but his heart and his thoughts were in Vienna. In 1952 at the age of 83 he astonished everyone by flying back to his native city, where he received a cordial official welcome. His happiness was complete. Unfortunately, before the end of that year he fell in his home and fractured his femur. Although physically incapacitated thereafter, he retained much of his mental activity until near the end.

I became acquainted with Neuburger early in the war years, and I was much impressed by the enthusiasm and the modesty of the man. He was an Honorary Fellow of the Royal Society of Medicine, and on December 1, 1943, we put out, for the meeting of the History Section on that day, a fairly complete exhibition of his printed books and papers in commemoration of his approaching 75th birthday. Neuburger was immensely touched. From 1946 until 1948 I was in much closer contact with him at the Wellcome Museum. He was still an ardent student, and his whole life was centred on the history of the healing art. He was by this time rather deaf and very myopic. Nine times out of ten, on opening the door of his room one found him poring over a book or a manuscript, using a reading-glass and with his head almost touching the page. Here in a flash was a vision of the mediaeval scholar. He never failed to express in many minor ways, sometimes unconscious, his gratitude to the people and the country that had given him freedom. His first article, in 1892, was on philosophy and medicine. A year ago he published what is possibly his last note, a brief article on the future of medicine based on its history. History and philosophy: these were the threads which ran unbroken through his long life.

In 1899 Neuburger married Johanna Conrad. They had two sons : the elder went to Tasmania in 1939, and the younger, Frederick, has been practising medicine in Buffalo, N.Y., since 1938. Frau Neuburger died in 1930. From his letters and from personal conversations it is evident that Neuburger was long and deeply affected by her death.

Dr. WALTER PAGEL writes: One of my earliest recollections is the photograph, on the drawing-room mantelpiece of my paternal home some 50 years ago, of a tall, martial figure in full Imperial Austrian court uniform, with plumed helmet, sword, and medals—and yet displaying the fine features of the scholar. It bore the familiar signature of Max Neuburger and was taken after his presentation to the Emperor when he had been appointed titular professor of medical history in the university of Vienna. Max

Neuburger was the last exponent of what may be called the "heroic" generation of medical historians. Its foremost exponents were Julius Pagel (1851–1912) and Karl Sudhoff (1853–1938). It was "heroic" because of the stupendous achievements which are due to these three men—and even more so because of the heavy odds against which they had to work at a time when historical studies in medicine were frowned upon and when there was no recognition of medical history as a subject for university teaching, departments, or research grants.

Of the three men, Sudhoff, as a practitioner well over 50, acquired an institute and, much later, a full professorship. Julius Pagel remained a practitioner throughout life, since his "extraordinary" professorship entitled him to lecture but not to "live." Neuburger, having been a practising neurologist, was given a full professorship and a department at the age of 50—yet his life before and after was a continual struggle with adversities. His stipend was always poor. He had to go through all the misery of post-war Vienna, when, hungry and cold, he wrote his masterpieces on the Vienna school in the kitchen of his flat in Neubaugasse. At the age of 70 he was subjected to the routine humiliations of Jewish scholars of highest standing at the "hearing" before an exalted member of the all-too-numerous Viennese Nazi mob. Finally, stripped of all earthly possessions, he found himself isolated from his children. This was the reward for nearly 50 years of devoted service and the sacrifices he had made for his department, to which he had given his precious library and collections. Neuburger was lucky in catching an aeroplane to London—the last leaving Vienna before war was declared.

A man of "great stature," erect and brave, Neuburger went through the London "Blitz" and a major operation—all the time working intensely and coming forward with ingenious ideas and unexpected finds. One such idea was to trace the personal contacts between British and Continental doctors, notably of the Vienna schools, and their repercussion on the development of medicine. All his works are classics of enduring vitality. Neuburger concentrated on the full presentation of subjects such as the history of neurophysiology (1897), the concept of the healing power of nature (1926), and indeed the whole of ancient and mediaeval medicine (1906–11)—rather than on the detection and first edition of manuscript sources (as Pagel and Sudhoff had done).

Neuburger was an idealist whose life may be fittingly inscribed with the conversion of a famous adage: "Primum philosophari, deinde vivere." Regardless of prospects and career he followed the creative spark in himself which had been kindled in his early schooldays by his headmaster, an inspiring teacher of history. Somewhat temperamental in disposition, he fearlessly and sincerely criticized friend and foe. Already in his earlier correspondence with such friends as Julius Pagel "saturnine" streaks of pessimism, impatience, and suspicion are recognizable. This was aggravated later on by the totalitarian attitude of Sudhoff, who, as Sigerist said, treated Neuburger unfairly. All this explains why recognition and honours meant much to Neuburger, especially in his later life—and it is gratifying that he lived to see himself rightly and universally hailed as the princeps of medical historians. It is with deep sorrow that we part from the last of a generation of fine scholars and great men.

Miss S. R. BURSTEIN, of the Wellcome Historical Museum, writes: Max Neuburger was essentially a social person; people were the staff of life to him. He delighted in the written recognition of his work or his birthdays. Quick to flare up in discussion, he sometimes offended people, but he was always sad if anyone dropped out of his life. An omitted greeting from anyone—be it colleague or cleaner—could darken his day. Yet he was capable of monumental patience. Venerating scholarship to the point of hero-worship, he was full of patience, sympathy, and kindness to the self-taught. To the younger generation he freely offered all the riches of his knowledge and experience. In historical biography he hated denigration of great characters, but he loved to seek out characters overlooked by history, especially those who seemed to have had their thunder stolen by greater personalities.

L. N. ROBINSON, C.B.E., M.D.

Dr. L. N. Robinson, formerly senior physician at the Hertford British Hospital in Paris, died at Reading on March 15, aged 85.

Leonard Nicholas Robinson was the son of Samuel Henry Robinson, of Howrah, Bengal. From Malvern College he went on to study medicine at Edinburgh, where he graduated M.B., C.M. in 1893, proceeding to the M.D. five years later. He was also a Doctor of Medicine of the University of Paris, where he continued his studies for some years and where he decided to live. In 1900 he was appointed physician to the Hertford British Hospital and he soon became widely known and respected both by his French colleagues and by the British residents in Paris. For some years he was senior member of the Medical Board for France of the Egyptian Civil Service, and in 1914 he was appointed president of the Paris Branch of the British Red Cross Society. During the first world war he served in the R.A.M.C. as a lieutenant-colonel and was mentioned in dispatches. He was appointed C.B.E. in 1920 and an officer of the Legion of Honour in 1933. He continued to practise in Paris (where his telegraphic address was the word Crusoe) until the second world war, when he returned to live in England. The last years of his retirement he spent at Biot in the Alpes Maritimes.

Dr. Robinson married Victoria, daughter of Mr. D. Hoef, in 1903, and he is survived by his widow and daughter.

We are indebted to Dr. C. G. JARVIS for the following appreciation: The passing away of Dr. Leonard N. Robinson further reduces the very small number of British practitioners in France. For many years he had been their respected and popular senior. He will be remembered for his manifold beneficent activities. For twenty-five years he was senior physician to the Hertford British Hospital in Paris. This institution was very near his heart and he gave it unstinted time and trouble. He was also a trustee of the British Charitable Fund and honorary physician to the British Legion, giving freely to all the benefit of his wisdom and experience.

When the first world war broke out he lost no time in organizing a local branch of the British Red Cross which rendered invaluable service. In the second world war he had settled near Exeter, where he acted as chairman of the West of England section of the Committee for British Subjects Evacuated from France. Here again he freely provided assistance and advice and strove to maintain constant contact between the exiles. After the war he retired to his pretty villa on the French Riviera. Unfortunately his eyesight gave him considerable trouble and this tribulation he keenly felt, for he was a great reader.

Robinson had in Paris a wide circle of friends, and many were those whom he had assisted and advised, for his kindness was proverbial. His always pleasant manner, his sense of humour, his utter lack of petty jealousy, and his readiness to help made him a very pleasant colleague. His devotion to duty was one of his predominating characteristics. He will long be remembered by those who were privileged to know him.

D. A. PRITCHARD, C.B.E., F.R.A.C.P., M.R.C.P.

Surgeon Rear-Admiral D. A. Pritchard, Director of Naval Medical Services in the Royal Australian Navy, died in Melbourne on March 11 at the age of 59.

Denis Adrian Pritchard was born at Stanmore, New South Wales, on April 26, 1895, and from Sydney

Grammar School he went on to Sydney University, where he studied science. During the first world war he came to Britain and worked as a scientist in munition factories. He returned to Sydney to study medicine, and graduated M.B., Ch.M. in 1922. In the following year he joined the Royal Australian Navy, in which he had a distinguished career. During the last war he served as squadron medical officer in H.M.A.S. *Perth* and *Australia*, and he was present at many Pacific actions. In 1946 he was appointed Director of Naval Medical Services and an honorary physician to the King. He was a Fellow of the Royal Australasian College of Physicians, and since 1935 had been a Member of the Royal College of Physicians of London. In 1952 he was appointed C.B.E. Surgeon Rear-Admiral Pritchard married Mary, daughter of Canon Harold Portis, and she survives him with their daughter.

Sir ALEXANDER FLEMING, M.D., D.Sc.
F.R.C.P., F.R.C.S., F.R.S.

Mr. A. G. CROSS, dean of St. Mary's Hospital Medical School, writes: Sir Alexander Fleming, to one who had known him as a teacher and later as a colleague, showed, apart from his scientific acomplishments, the two outstanding characteristics of modesty and of great loyalty both to St. Mary's Hospital Medical School and to the Wright–Fleming Institute, of which he had been director. He accepted all the honours which came to him as a result of the discovery of penicillin in a spirit of incredulity and with the suggestion that he was not really deserving of all these tributes. He was always ready to undertake any task for the medical school and was a constant supporter of the students in all their activities. A keen swimmer and a good shot in his younger days, he was for many years a regular supporter of the rugger and cricket teams, and he was always interested in the results of the various inter-hospital competitions. The world by his death has lost a great benefactor and St. Mary's has lost a loyal friend.

Mr. H. H. DU BOULAY, honorary consulting surgeon to the Weymouth and Dorset County Royal Eye Infirmary and to the Weymouth and District Hospital, died at Chandler's Ford, Hampshire, on March 1 at the age of 94. The eldest son of the Rev. J. T. H. Du Boulay, Hubert Houssemayne Du Boulay was born on December 8, 1860, and was educated at Winchester College, where his father was a house-master. He received his medical training at Guy's Hospital and qualified by taking the M.R.C.S. in 1885 and the L.R.C.P. in the following year. After qualification he studied ophthalmology at Leeds, and then, in 1889, he settled in general practice at Weymouth in partnership with Dr. Christopher Childs, and soon afterwards was appointed assistant surgeon to the Weymouth and Dorset County Royal Eye Infirmary. A little later he became general surgeon at the Royal Hospital, Weymouth, where he worked in close association with the late Dr. P. S. B. Wetherall. In 1921 he, together with Dr. Wetherall, Dr. J. Macpherson Lawrie, and Dr. T. H. Sanderson-Wells, was instrumental in amalgamating the Royal Hospital with the Princess Christian Hospital, to become the Weymouth and District Hospital. When he retired from practice in 1924 he became consulting surgeon to the eye infirmary and to the hospital. He then went to live at Chandler's Ford, returning to Weymouth in 1925 to receive the freedom of the borough, and at the time of his death he was the borough's oldest surviving freeman. During the 35 years he was at Weymouth Dr. Du Boulay became a well-known and respected figure. Many years ago he created something of a sensation when he gave up wearing the conventional medical attire of frock-coat and top hat and appeared in an ordinary suit with a bowler hat. Although he practised as a general physician and surgeon he was particularly interested in ophthalmology, and for a long time he was the only ophthalmologist in the town. He never accepted the panel system and always continued in private practice. He was much better known as an ophthalmologist in south Dorset than a general practitioner, and it is chiefly through his association with the eye infirmary at Weymouth that he is remembered. An associate brother of the Venerable Order of St. John of Jerusalem, he was a lecturer to the St. John Ambulance Brigade and to the ambulance classes of the local railways, and during most of the time he was at Weymouth he acted as surgeon to the old Great Western Railway's provident society. A widower for many years, he devoted much care to his invalid wife during her lifetime. He is survived by two sons, both of whom live in Canada.

Dr. E. VIPONT BROWN, who was in general practice at Manchester for over fifty years, died on February 26 at his home at Yealand Conyers, near Carnforth, Lancashire, where he had been living in retirement since the end of the second world war. He was 92 years of age. Edward Vipont Brown was born at North Shields on February 12, 1863, and was educated at Bootham School, York, where he matriculated in 1880, and at Owens College, Manchester. He then entered St. Bartholomew's Hospital Medical College as a medical student and qualified by taking both the M.R.C.S. and L.S.A. diplomas in 1886. In later life he enjoyed telling how he and other Bart's students would absent themselves from lectures at their own medical school in order to listen to Sir Joseph (later Lord) Lister, who was then teaching at King's, a procedure which, understandably enough, annoyed the professor of surgery at St. Bartholomew's. Pursuing his studies after qualification, he obtained the London M.B. in 1888 and proceeded to the M.D. in 1901. Dr. Vipont Brown settled at Manchester in 1894 in partnership with his brother-in-law, the late Dr. Owen Gwatkin, but the latter had to leave the district soon afterwards for health reasons, and Dr. Vipont Brown succeeded to the practice and soon proved himself to be a good and reliable doctor. In time many of his patients were of the second and often the third generation of the same family, and all came to regard him not only as a doctor but as a friend in whom they could place full confidence and to whom they could always appeal for help. Throughout his long life Dr. Vipont Brown, who was a Quaker, worked hard as a disciple of peace, and he was keenly interested, also, in the temperance movement, being himself a lifelong abstainer, while, as one who attended postgraduate classes until he was in his seventies, it was perhaps natural that he should give his encouragement to adult education. Possessed of the gift of speech, he was in demand as a speaker not only by the Society of Friends but by other denominations as well. All these interests were reflected in his writings. As long ago as 1902 he wrote on Christianity and war, and in other publications he discussed the Quaker aspects of truth, the medical aspects of the temperance question, the effects of alcohol as seen by medical men, and instinct, intelligence, and religion. He became a member of the Manchester Medical Society in 1887 and was a familiar figure at its meetings until he retired at the age of 82. He was auditor of the society in 1894, a member of its committee in 1899, and a vice-president in 1920. A member of the British Medical Association for over sixty-five years, he represented Manchester (South) at the Annual Representative Meeting held at Belfast in 1909. Dr. Vipont Brown was always extremely active and busy. While at school he held the record for the mile, and in his youth cycled from York to Edinburgh on a "penny-farthing" machine. As a young practitioner he usually used a horse and trap to visit his patients, but up to an advanced age he could be seen riding his bicycle, for motor-cars never appealed to him and he could never learn how to drive one. He had the happiness to live long enough to celebrate his diamond wedding anniversary in January this year, and is survived by his widow, formerly Miss Dorothy Crowley, whom he married in 1895. His son carries on the practice at Manchester.

Medico-Legal

FORGOTTEN SWAB

In the Queen's Bench Division on March 15 Mr. Justice Pearson gave judgment for £3,000 damages in favour of Mrs. E. B. J. Urry, aged 31, of Maidenhead, against Mr. Immanuel Bierer, gynaecological surgeon, of London, W.1, and the proprietors of the Harley Street Nursing Home in respect of a caesarean operation at the nursing-home on January 7, 1953. Mrs. Urry complained that a pack about 10 in. (25 cm.) square was left inside her, necessitating an operation on January 13 for its removal.

The defendants denied any negligence. A similar action against the surgeon who assisted at the operation, Dr. Max Odens, was dismissed with costs awarded to him.

Mr. Justice Pearson, giving judgment, said the nursing-home and the theatre sister, Mrs. Gwendolen Cole, had and deserved to have the highest reputation. Mr. Bierer had long and wide experience and held a number of appointments. The nursing-home provided the packs. Mr. Bierer had not operated at the nursing-home before nor had he operated with the same theatre sister. His Lordship said the surgeon normally asked the theatre sister if swabs were correct. Then there was what might be called the ritual of the sister's count of the used packs together with any outstanding pack or packs left for the surgeon's use later. Mrs. Cole's evidence was that on this occasion there were eleven used packs and one available for Mr. Bierer. Mrs. Cole and her assistant both counted the packs audibly, and Mrs. Cole ended by pointing out the twelfth and last pack, which was available for Mr. Bierer. The judge said his view on the balance of probabilities was that it was a pre-count pack which was left behind. On that assumption, it followed that there was an error in the count, and it had been admitted that on that finding there was negligence and the nursing-home was liable.

Mr. Bierer had agreed, said the judge, that the surgeon had a duty to take reasonable precautions against leaving a pack behind, but thought that duty was performed by relying solely and exclusively on the sister's count of the swabs. His lordship found that it was not proved that that was in accordance with any approved practice. The sister's count was fallible, and some other precaution was needed. The fact that some other precaution was also fallible was not a sufficient reason against adopting it. Both Mr. Bierer and the theatre sister failed in their respective duties, and if either duty had been performed the pack would not have been left behind. There was no reason to divide the responsibility other than equally. Mrs. Urry's pain and suffering had been very great, and there would be a third operation to remove the scar and internal adhesions. There was some hope that physically she would be completely cured. Psychologically there had been terrible damage.

His lordship entered judgment against Mr. Bierer and the nursing-home for Mrs. Urry for £3,000 damages with costs. On a counter claim by the nursing-home for fees judgment was entered for £270 against the plaintiff's husband, Mr. Urry, who was given judgment for £1,146 as agreed special damages. A stay of execution with regard to £2,000 of the damages awarded to Mrs. Urry was granted pending the consideration of an appeal.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for Mr. Bierer and Dr. Odens.

HOSPITAL BOARD PAYS UP

In 1950 and 1951 a radiologist was employed by the South-west Metropolitan Regional Hospital Board as a part-time locumtenent consultant radiologist at various hospitals. On a number of occasions he was engaged to and did undertake a total of more than nine sessions per week, when he was employed in two or more such locumtenent posts concurrently. When he asked for payment at the rate of 3½ guineas for each session he was told that under paragraph 7 of the Terms and Conditions of Service of Hospital Medical and Dental Staff (England and Wales) and by virtue of a Ministry of Health circular R.H.B. 49 (115) he was not entitled to be paid for more than nine sessions in any week, however many he had actually performed. As a result the board withheld the sum of £102 18s. from his remuneration. After considerable correspondence the radiologist issued a writ against the board. He has now been informed that the board proposes to pay his claim in full.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for the radiologist.

Medical Notes in Parliament

Teething Powders

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Health what advice he had received on the association of mercury poisoning in infants, following the ingestion of teething powders or tablets containing mercury, with pink disease; how many infants had died within the last two years from pink disease, and how many from mercurial poisoning; and in how many cases both factors applied. Mr. IAIN MACLEOD, replying on March 14, said he was advised that the degree of association between mercury poisoning and pink disease had not been clearly established. Many cases of pink disease had no demonstrable association with ingestion of mercury, and the great majority of children who had been given mercurial preparations showed no sign of the disease. It seemed possible that some few infants might have an exceptional sensitivity to mercury. In 1952 and 1953, 64 children under 5 years old were certified as dying from pink disease, and 4 from mercury poisoning; in 2 cases both pink disease and mercury poisoning were mentioned in the death certificate.

Pneumoconiosis Diagnosis

Mr. W. N. WARBEY (Broxtowe, Lab.) asked the Minister of Pensions and National Insurance whether he would institute an inquiry into the causes of the wide variation in the proportion of pneumoconiosis claims diagnosed as such by the pneumoconiosis medical panels in the different areas. Mr. OSBERT PEAKE replied on March 14 that he did not think the inquiry suggested would serve any useful purpose. Mr. WARBEY said that the wide variation was causing a good deal of unrest in the mining industry. It was as high as 78% in Scotland and 70% in the West Midlands, and as low as 47% in the East Midlands. Now that the scheme had been working for some years would it not be a good thing to have an inquiry, both into the diagnostic criteria and into the question whether it was really a good thing to have a panel of medical experts functioning as a final appeal tribunal for claims to benefit? Mr. PEAKE said that he could not accept that the proportion of successful claims in different districts showed that there was any wide variation in diagnosis in those districts. Conditions giving rise to the disease, the form of the disease itself, and the awareness of the risk of disease, varied greatly from district to district.

1914–18 War Pensioners

Mr. C. J. SIMMONS (Brierley Hill, Lab.) on March 14 asked the Minister of Pensions and National Insurance whether he had considered the opinion expressed in the Report of the Rock Carling Committee that some limbless and other seriously wounded men of the 1914–18 war found their disabilities more burdensome in advancing years, and had now reached a stage deserving of reconsideration; and what action he proposed to take in this matter. Mr. OSBERT PEAKE said that he was always willing to review the case of any war pensioner who applied to have his assessment reconsidered on the ground that his war disablement had grown worse. There were, he also said, 23,000 limbless pensioners, and 356 increases of assessment had been made between the

merger of the Ministries of Pensions and National Insurance in September, 1953, and the end of 1954. There were 144,000 other wounded from the first world war, and 1,000 had been given increases.

Factory Accidents

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Labour on March 15 whether he had noted the unsatisfactory figures for the number of accidents that occurred among women and girls in factories and establishments supervised by the Inspectorate of Labour; and what steps were being taken to bring the accident rate among these groups to a lower level. Mr. HAROLD WATKINSON, the Parliamentary Secretary, replied that the Chief Inspector of Factories again drew attention to the unsatisfactory trend of these accidents in his last annual report, and urged that industry should devote more thought to means of reducing the number of accidents to female workers. Inspectors of factories paid attention to this problem in their inspections of establishments employing female workers. The National Joint Advisory Council had appointed a subcommittee to make recommendations on the means by which greater freedom from accidents to workpeople generally might be achieved. He would not agree with a submission by Dr. Stross that the inspectorate tended to become grossly weakened year by year in the technical skill of its entrants. It was, he said, a special problem that had been clearly outlined, and there was an expert subcommittee working on it. He agreed with Mr. F. LEE (Newton, Lab.) that more safety committees inside some types of factory would do a great deal to help.

Vole Vaccine

Mr. JOHN RANKIN (Glasgow, Tradeston, Lab.) asked the Secretary of State for Scotland on March 15 if he had reached any conclusions as to the effectiveness of vole vaccine in the treatment of tuberculosis, as the result of the inoculations given to the children at Bridge of Weir Home. Mr. J. STUART replied that vole vaccine, like B.C.G. vaccine, was a protection against tuberculosis, not a form of treatment. So far as could be established by testing all those who were vaccinated, the effectiveness of the two vaccines was closely comparable. There had been no cases of tuberculosis in the Homes since vaccination began in 1951.

Helicopter Ambulance

Mr. J. GRIMOND (Orkney and Zetland, L.) asked the Secretary of State for Scotland on March 15 if he would arrange for a helicopter to be available in cases of emergency for serious medical cases in the Highlands, especially in islands on which the present air ambulance could not land. Mr. J. STUART said that while he was advised that there were risks in using single-engined helicopters on overwater crossings, he was considering with the First Lord of the Admiralty the extent to which use could be made of naval helicopters in extreme medical emergencies.

Resettlement in Malaya

Mr. H. HOPKINSON, Minister of State, Colonial Office, stated in answer to Mrs. LENA JEGER (Holborn and St. Pancras South, Lab.) on March 16, that every resettlement village in Malaya had either a dispensary or a maternal and child health centre. In 1954 medical work in these "New Villages" was provided for by grants of $2,500,000 to the Governments of the States and Settlements, and $1,350,000 to the Red Cross, the St. John Ambulance Brigade, and the missions, all of which had since 1952 been making a magnificent contribution under emergency conditions in the rural areas.

Food and Drugs Act.—The date of bringing into operation the Food and Drugs Amendment Act has not yet been decided, but the Minister intends to bring it into force as soon as possible.

Industrial Diseases.—The Beney Committee appointed to inquire into industrial diseases not covered by the Industrial Injuries Acts is understood to be working on its report.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **March 5** (No. 9) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	17	1	4	0	1	34	1	7	0	1
Dysentery	1,265	64	322	17	8	1,007	94	276	12	5
Encephalitis, acute	5	0	0	0		5	0	0	0	-
Enteric fever:										
Typhoid	3	0	1	0		1	0	0	0	
Paratyphoid	5	0	0	1		15	1	1	0	
Food-poisoning	111	17		4*		194	12		0	
Infective enteritis or diarrhoea under 2 years				15	16				12	32
Measles*	26,453	3412	361	605	169	2,449	33	82	19	395
Meningococcal infection	32	0	12	1	5	27	3	17	0	
Ophthalmia neonatorum	37	4	6	0		24	0	2	1	
Pneumonia†	954	72	279	41	8	709	31	254	9	2
Poliomyelitis, acute:										
Paralytic	11	1	2	0	1	14	1	4	0	
Non-paralytic	3	1				4	0			
Puerperal fever§	235	48	6	1		241	39	12	0	
Scarlet fever	648	19	79	51	31	1,379	51	181	40	33
Tuberculosis:										
Respiratory	716	70	122	18		740	109	150	21	
Non-respiratory	96	7	26	3		128	7	23	3	
Whooping-cough	1,834	145	167	53	22	2,034	94	385	45	44

DEATHS in Great Towns	1955					1954				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	1
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	18	1	1	1	0	15	1	1	1	3
Influenza	70	11	5	3	6	26	1	2	0	0
Measles		2	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	449	66	53	26	12	323	51	28	10	5
Poliomyelitis, acute	2	0			0	1	0			0
Scarlet fever		0	1	0	0		0	0	0	0
Tuberculosis:										
Respiratory	107	19	14	0	6	129	17	18	4	6
Non-respiratory		0	0	0	0		1	1	0	2
Whooping-cough	1	0	0	0	0	3	0	1	0	0
Deaths 0–1 year	231	41	39	15	9	275	28	28	5	15
Deaths (excluding stillbirths)	8,032	1139	879	200	285	6,457	868	707	125	201
LIVE BIRTHS	8,050	1144	976	208	318	8,009	1181	904	227	399
STILLBIRTHS	231	12	18			207	23	26		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Infectious Diseases

The only large variations in the trends of the notifications of infectious diseases in England and Wales during the week ending March 5 were increases of 2,753 for measles, from 23,700 to 26,453, and 160 for whooping-cough, from 1,678 to 1,838.

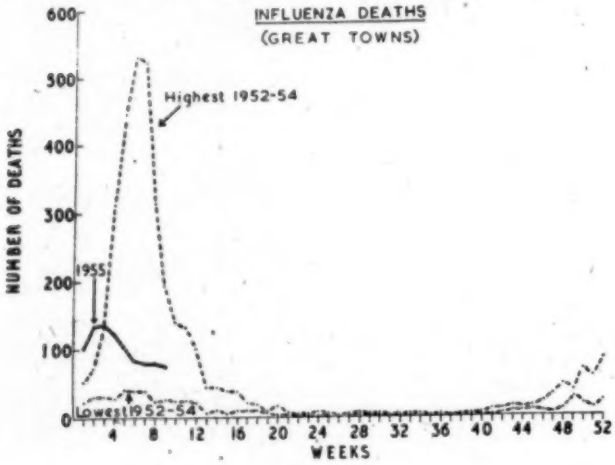
The largest increases in the incidence of measles were 718 in London, from 2,694 to 3,412, 551 in Yorkshire West Riding, from 3,335 to 3,886, 446 in Kent, from 986 to 1,432, 346 in Essex, from 1,392 to 1,738, 224 in Derbyshire, from 998 to 1,222, 195 in Warwickshire, from 1,579 to 1,774, 192 in Surrey, from 807 to 999, 192 in Middlesex, from 616 to 808, 146 in Nottinghamshire, from 1,275 to 1,421, and the only large fall was 124 in Hertfordshire from 319 to 195. 648 cases of scarlet fever were notified, being 27 fewer than in the preceding week, and no large variations were recorded in the trends. The largest rises in the incidence of whooping-cough were 53 in Lancashire, from 158 to 211, and 35 in Kent, from 80 to 115. 17 cases of diphtheria, 4 more than in the preceding week, were notified.

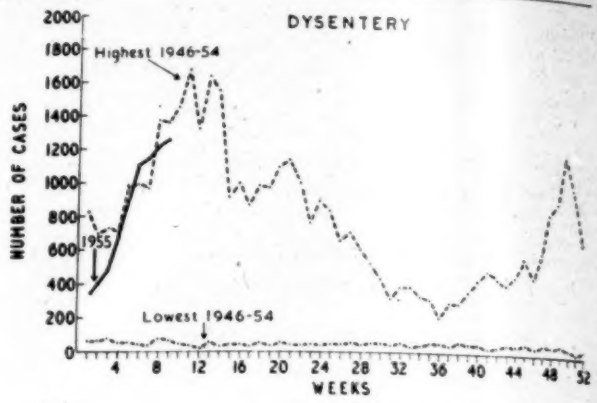
14 cases of acute poliomyelitis were notified. These cases were 2 more for both paralytic and non-paralytic cases than in the preceding week. The multiple notifications were Yorkshire West Riding 5 (Leeds C.B. 2) and London 2.

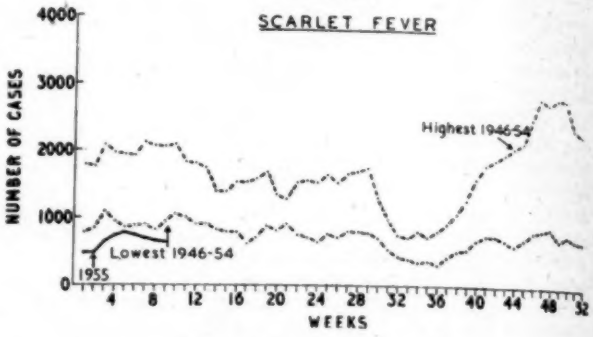
For the ninth consecutive week a rise has been reported in the number of notifications of dysentery. During the week reviewed 1,265 cases were notified, an increase of 28. The largest returns were Lancashire 524 (Blackpool C.B. 155, Oldham C.B. 115, Blackburn C.B. 102, Manchester C.B. 30, Liverpool C.B. 20, Royton U.D. 18, St. Helens C.B. 12, Chadderton U.D. 12, Darwen M.B. 12, Lytham St. Anne's M.B. 12), Northumberland 95 (Newcastle-upon-Tyne C.B. 30, Morpeth M.B. 19, Whitley Bay, M.B. 17), Yorkshire West Riding 85 (Huddersfield C.B. 29, Leeds C.B. 21), London 64 (Chelsea 9), Durham 62 (South Shields C.B. 10, Easington R.D. 10, Lanchester R.D. 10), Norfolk 50 (Norwich C.B. 30), Northamptonshire 47 (Northampton C.B. 31, Kettering M.B. 13), Leicestershire 37 (Leicester C.B. 24), Cheshire 37 (Stockport C.B. 22), Surrey 27 (Egham U.D. 13), Nottinghamshire 26 (Beeston and Stapleford U.D. 12, East Retford M.B. 10), Glamorganshire 26, and Yorkshire North Riding 20 (Middlesbrough C.B. 19).

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the nine years 1946–54 (influenza, 1952–4) are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Week Ending March 12

The notifications of infectious diseases in England and Wales during the week included : scarlet fever 780, whooping-cough 1,881, diphtheria 9, measles 25,321, acute pneumonia 958, acute poliomyelitis 11, dysentery 1,407, paratyphoid fever 8.

Universities and Colleges

UNIVERSITY OF OXFORD

Theodore Williams Scholarships in Pathology have been awarded to Margaret R. Blears (Lady Margaret Hall) and Rosemary E. Troughton (Scholar of Somerville College).

In Congregation on January 20 the following medical degrees were conferred :

B.M.—W. G. Cowell, C. S. K. Ruck, D. Severs, Audrey M. Grumitt, and G. D. H. Lynne-Davies (in absence).

UNIVERSITY OF LONDON

In Convocation on January 8 it was announced that Dr. Patricia M. Elliott had been elected and Dr. C. A. H. Franklyn re-elected as representatives of the Faculty of Medicine on the Standing Committee of Convocation for a period of three years.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

Drs. W. R. Shanahan and O. M. P. Tobias were admitted to the Membership of the College on February 4 and Dr. K. M. Basu on March 4 (*in absentia*).

The Services

The *London Gazette* has announced the following awards:

Third Clasp to the Territorial Efficiency Decoration.—Brigadier A. L. Crockford, D.S.O., O.B.E., M.C., T.D., Q.H.S. (Honorary Colonel of a T.A. Unit).

Second Clasp to the Territorial Efficiency Decoration.—Major J. E. Elliott, T.D., R.A.M.C.

First Clasp to the Territorial Efficiency Decoration.—Captain (Honorary Major) H. E. Blake, R.A.M.C.

Territorial Efficiency Decoration.—Colonel R. W. Raven, O.B.E., Major (Honorary Lieutenant-Colonel) J. H. Haslett, Majors H. W. W. Good and G. H. Smith, Captains (Honorary Majors) E. W. O. Adkins, H. E. Blake, and H. S. Shucksmith, and Captain J. C. Cameron, R.A.M.C.

Medical News

Tetracycline on Prescription.—The Ministry of Health, Department of Health for Scotland, and Ministry of Health and Local Government, Northern Ireland, have arranged with the manufacturers concerned for tetracycline to be available on prescription from April 4. The Health Departments are advised by the Medical Research Council that tetracycline is suitable for the treatment of the same conditions as chlortetracycline ("aureomycin") and oxytetracycline ("terramycin"), and its toxicity is also similar, so that the same precautions should be observed in its employment (see the statement prepared by the Medical Research Council and printed in the *Journal* on October 23, 1954, p. 984).

Committee on Homosexuality and Prostitution.—The special committee of the B.M.A. which is preparing evidence for submission to the Departmental Committee on Homosexuality and Prostitution is considering whether there is any relationship between endocrine factors and some forms of homosexuality. For this purpose it wishes to invite the co-operation of medical practitioners who have among their patients homosexuals prepared to answer certain questions. Will any practitioner willing to assist kindly communicate with the Secretary of the Association, B.M.A. House? All information obtained will be regarded as confidential and anonymity will be preserved. The Secretary would also be glad to hear from practitioners with experience or information relevant to the committee's work.

David Anderson-Berry Prize.—The Royal Society of Edinburgh invites application for the 1956 David Anderson-Berry Prize, consisting of a silver-gilt medal and a sum of about £100. The prize will be awarded to the person who, in the opinion of the council of the Society, has recently produced the best work on the therapeutic effect of *x* rays on human diseases. Applications, which may be based on both published and unpublished work, must be in the hands of the secretary of the Royal Society of Edinburgh, 22, George Street, Edinburgh, 2, by March 31, 1956.

Alan Newton Prize.—The Royal Australasian College of Surgeons announces that the subject for the next Alan Newton Prize essay will be "The Pathogenesis and Surgical Treatment of Developmental Abnormalities of the Kidneys and Ureters." The prize is awarded biennially and is open to Fellows of the Royal Colleges of Surgeons of Australasia, England, Edinburgh, and Ireland, and to Fellows in Surgery of the Royal Faculty of Physicians and Surgeons of Glasgow. Essays, not exceeding 75,000 words in length, must reach the secretary of the Royal Australasian College of Surgeons (from whom further details may be obtained), Spring Street, Melbourne, C.1, by December 1, 1956.

Butterworth Gold Medal.—This is an award to be presented annually to the College of General Practitioners by Messrs. Butterworth and Company, the medical publishers, for an essay by a member or associate of the College on a subject connected with general practice. The subject for this year's essay is "The Influence of Home Conditions during the First Five Years of Life on the Physical and Mental Health of Children." Essays, identified by motto only and not exceeding 10,000 words, should be submitted to the chairman of the Awards Committee, College of General Practitioners, 14, Black Friars Lane, London, E.C.4, not later than September 30.

Buckston Browne Prize Essay.—The council of the Harveian Society of London has chosen "Hypertension" as the subject for the next Buckston Browne Prize Essay. The prize, consisting of a medal and £100, is open to any member of the medical profession "registered in the British Isles or Dominions" under the age of 45. The closing date for the receipt of essays is August 31, 1956. Further details from the hon. secretaries of the society, 11, Chandos Street, Cavendish Square, London, W.1.

Welsh National School of Medicine.—Dr. A. T. JONES, senior administrative medical officer of the Welsh Regional Hospital Board, has been appointed Provost of the Welsh National School of Medicine in succession to Professor R. M. F. PICKEN, who is due to retire on September 30.

Chair of Biochemistry, Sheffield.—Dr. Q. H. GIBSON, at present reader in physiology at Sheffield, has been appointed to the vacant chair of biochemistry from April 1. He succeeds Professor H. A. Krebs, F.R.S., who left on his election last year to the Whitley Professorship of Biochemistry at Oxford. Dr. Gibson graduated at Queen's University, Belfast, in 1941, and from 1941 to 1947 was successively demonstrator and lecturer in physiology at Queen's. In 1947 he moved to the department of physiology at Sheffield. He is particularly interested in haemoglobin, and has published important papers on methaemoglobinaemia.

Glasgow Medical Graduates near Sheffield.—Will those interested in forming a Sheffield Region Glasgow University Male Medical Graduates Association communicate with Dr. E. MILLAR, 5, Far Lane, Sheffield, 6?

National Spastics Society.—The society made £270,000 from its Christmas sales appeal at the end of last year. The appointment is now announced of a director-general (Lieutenant-Commander I. R. HENDERSON) to "direct and co-ordinate the increasing work of the society in connexion with its big development programme to help spastic children by opening new treatment centres and clinics throughout the country."

Sir Russell Brock has been awarded the West London Medico-Chirurgical Society's triennial gold medal. It will be presented to him at the annual banquet of the society on June 23 at the Royal College of Surgeons.

Sir Godfrey Huggins, C.H., F.R.C.S.—On February 26 we reported (p. 550) that the Queen had approved the conferment of a viscountcy on Sir Godfrey Huggins, Prime Minister of the Federation of Rhodesia and Nyasaland. The name, style, and title are now announced as Viscount Malvern, of Rhodesia and of Bexley in the County of Kent.

COMING EVENTS

Edinburgh Medical Exhibition.—Professor D. M. DUNLOP will open the Edinburgh Medical Exhibition at the Assembly Rooms, George Street, at 11.30 a.m. on April 25. The exhibition will be open daily, 11 a.m. to 6.30 p.m. (7.30 p.m. on April 27), until April 29.

Fertility and Sterility.—Second World Congress will be held in Naples, May 18–26, 1956. Those wishing to contribute papers should get in touch with Dr. G. I. M. SWYER, Obstetric Hospital, University College Hospital, Huntley Street, London, W.C.1.

European Society of Cardiovascular Surgery.—The Fourth Congress will be held at Copenhagen on July 28 and 29, during the week of the International Society of Surgery. On the first day there will be a discussion on "Surgical Treatment of Chronic Pericarditis," and on the second a symposium on angiology will be held with the International Society of Surgery. The subjects of communications and discussions must be received before April 15 by the secretary-general—Dr. G. ARNULF, 41, rue Sainte-Hélène, Lyon, France. The local secretary of the Congress is Dr. A. Gammeltoft, Københavns Amts Sygehus, Copenhagen, to whom application for accommodation in Copenhagen should be made as soon as possible.

Association of Sea and Air Port Health Authorities.—The annual meeting will be held in London, June 8–10. Details from the hon. secretary, Dr. H. C. MAURICE WILLIAMS, Health Department, Civic Centre, Southampton.

NEW ISSUES

British Journal of Pharmacology and Chemotherapy.—The new issue (Vol. 10, No. 1) is now available. The contents include:

THE MODE OF ACTION OF ANTITHYROID DRUGS: FURTHER OBSERVATIONS ON IN VITRO INHIBITION OF OXIDATIVE PROTEIN IODINATION. Russell Fraser, M. G. W. Hanno, and W. R. Pitney.

IN VITRO TESTS OF CHEMICAL COMPOUNDS ON ASCARIS LUMBRICOIDES AND FASCIOLA HEPATICA. A. Mackie, G. Marjorie Stewart, A. A. Cutler, and A. L. Misra.

THE EFFECT OF ANTI-CHOLINESTERASE AGENTS ON THE RAT'S BLOOD PRESSURE. P. Dirnhuber and H. Cullumbine.

STUDIES ON THE TOXICITY OF ALKYL TIN COMPOUNDS. H. B. Stoner, J. M. Barnes, and Janet I. Duff.

A CORRELATION BETWEEN CHOLINESTERASE INHIBITION AND INCREASE IN MUSCLE TONE IN RABBIT DUODENUM. Heather Shelley.

THE ISOLATED HEART OF *MYA ARENARIA* AS A SENSITIVE PREPARATION FOR THE ASSAY OF ACETYLCHOLINE. Brodie Hughes.

THE EFFECTS OF ADRENALINE, NORADRENALINE, AND DIHYDROERGOTAMINE ON EXCISED HUMAN MYOMETRIUM. William J. Garrett.

THE EFFECT OF NALORPHINE ON THE ANTIDIURETIC ACTION OF MORPHINE IN RATS AND MEN. H. Schnieden and E. K. Blackmore.

HISTAMINE RELEASE AND THE "STRESS" PHENOMENON. P. A. Nasmyth.

THE FORMALDEHYDE DERIVATIVES OF AMINO ACIDS AND THE MODE OF ACTION OF A FORMALDEHYDE-TYROSINE DERIVATIVE AGAINST INFLUENZA A VIRUS IN OVO. Lois Dickinson.

THE ACTION OF LYSERGIC ACID DIETHYLAMIDE ON MAMMALIAN CHOLINESTERASES. R. H. S. Thompson, A. Tickner, and G. R. Webster.

CARDIOVASCULAR AND RESPIRATORY ACTIONS OF 5-HYDROXYTRYPTAMINE IN THE CAT. S. R. Kottegoda and Joan C. Mott.

ANTITUBERCULOUS EFFECTS OF CERTAIN SURFACE-ACTIVE POLYOXYETHYLENE ETHERS. J. W. Cornforth, P. D'Arcy Hart, G. A. Nicholls, R. J. W. Rees, and J. A. Stock.

HISTAMINE RELEASE IN RABBIT BLOOD BY DEXTRAN AND DEXTRAN SULPHATE. C. G. Haining.

THE SPASMOLYTIC PROPERTIES OF THIOBENZILIC ACID ESTERS AND RELATED COMPOUNDS. M. W. Parkes.

THE EFFECT OF COMPOUND 48/80 ON GANGLIONIC TRANSMISSION. S. B. Gertner.

THE EFFECTS OF SODIUM SALICYLATE ON BLOOD GLUCOSE IN THE RAT. M. J. H. Smith.

THE THERAPEUTIC ACTIVITY OF SOME SULPHONES AND SULPHOXIDES IN EXPERIMENTAL TUBERCULOSIS OF GUINEA-PIGS. S. K. Gupta and R. N. Chakravarti.

OBSERVATIONS ON Ω-AMINO-POLYMETHYLENE TRIMETHYLAMMONIUM COMPOUNDS. R. B. Barlow, H. Blaschko, Jean M. Himms, and U. Trendelenburg.

THE ACTIONS OF HETEROCYCLIC BISQUATERNARY COMPOUNDS, ESPECIALLY OF A PYRROLIDINIUM SERIES. D. F. J. Mason and R. Wien.

Issued quarterly; annual subscription £4 4s.; single copy 25s.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, March 28

INSTITUTE OF ORTHOPAEDICS.—5 p.m., Dr. W. R. Bett: Medical Writing—The Use of Medical Libraries and the Preparation of Papers for Medical Journals.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion to be introduced by Dr. J. T. Ingram and Dr. C. Allan Birch: Cutaneous Manifestations of General Disease.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. E. G. Muir: Treatment of Cancer of the Rectum; 6.30 p.m., Mr. N. R. Barrett: Mediastinal Tumours.

Tuesday, March 29

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. M. F. Bishop: Steroid Therapy.

MIDDLESEX COUNTY MEDICAL SOCIETY.—At North Middlesex Hospital, Silver Street, Edmonton, N., 3 p.m., clinical meeting.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. Rodney Smith: Treatment in Acute Intestinal Obstructions; 6.30 p.m., Professor R. McWhirter: Tumours of High Radiosensitivity.

ROYAL STATISTICAL SOCIETY: STUDY CIRCLE ON MEDICAL STATISTICS.—At Westminster Medical School, 6 p.m., Dr. C. J. Donelan, Dr. K. W. Cross, and Professor R. M. Titmuss: Hospital Statistics: A Discussion of Ends and Means.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. G. C. Knight: Diagnosis and Treatment of Facial Pain and Trigeminal Neuralgia.

Wednesday, March 30

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Trends in the Study of Mycotic Diseases.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. E. G. B. Calvert: Surgery and the Diabetic.

LONDON UNIVERSITY.—At St. Thomas's Hospital Medical School, 5 p.m., special university lecture in pharmacology by Professor Mark Nickerson (Manitoba): Specific Inhibition of Adrenergic Responses.

MANSFIELD MEDICAL SOCIETY.—At Mansfield and District General Hospital, 8.30 p.m., Dr. C. M. Fletcher: Miners' Lung. Members of the Nottinghamshire Branch, B.M.A. are invited.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Erasmus Wilson Demonstration by Dr. J. Stretton Young: Degeneration in Tumour Pathology.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Professor R. S. Pilcher: Pathology and Treatment of Bronchiectasis; 6.30 p.m., Mr. D. J. Browne: Congenital Dislocation of the Hip.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. J. Minton: Prevention of Blindness in Infancy and Childhood (illustrated).

ST. MARYLEBONE HOSPITAL FOR PSYCHIATRY AND CHILD GUIDANCE.—5.30 p.m., Dr. J. Flind: Psychosomatic Disorders.

Thursday, March 31

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. W. R. Bett: Medical Writing.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., annual meeting; 8.30 p.m., Mr. R. Roaf: Hospitals and Medical Schools in India.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. B. E. Schlesinger: Indications for Cortisone Therapy in Paediatrics.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.30 p.m., Otolaryngology Lecture by Professor Lambert Rogers: Vascular Diseases in Relation to Otolaryngology.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—6.30 p.m., Mr. T. Holmes Sellors: Constrictive Pericarditis.

ROYAL EYE HOSPITAL.—5.30 p.m., Dr. T. H. Whittington: Some Aspects of Refraction Work: (6) Hypermetropic and Myopic Patients Compared.

SOCIETY OF ANAESTHETISTS OF SOUTH WALES.—At Seabank Hotel, Porthcawl, 7.30 for 8 p.m., (1) Dr. E. Harvey Franks: Intra-arterial Thiopentone; (2) Professor W. W. Mushin: Trilene Analgesia in Midwifery; (3) Dr. W. W. Mapleson, Ph.D.: Things Aren't Always What They Seem; (4) Dr. H. G. Middleton: Anaesthesia in the Treatment of Burns.

Friday, April 1

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., radiological demonstration by Dr. Franklin G. Wood.

●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. N. C. Tanner: Treatment of Cancer of the Stomach; 6.30 p.m., Mr. E. W. Riches: Retention of Urine.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: WELSH BRANCH.—At B.M.A. House, 195, Newport Road, Cardiff, 6.30 p.m., joint meeting with West of England Industrial Medical Officers. Discussion: Foot Hygiene. Speakers, (a) Mr. Gwyn James, (b) an Industrial Medical Officer, (c) a representative of the British Boot, Shoe, and Allied Trades Research Association.

WHITTINGTON CLINICO-PATHOLOGICAL SOCIETY.—At Archway Wing, Whittington Hospital, N., 5.15 p.m., demonstration by Dr. A. L. Jacobs. Illustrated lecture by Mr. W. W. Davey: Is Your Gastrectomy Really Necessary?

Saturday, April 2

MIDLAND TUBERCULOSIS SOCIETY.—At King Edward VII Memorial Sanatorium, Hertford Hill, near Warwick, 3 p.m., clinical meeting and annual general meeting.

APPOINTMENTS

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—Aileen B. Donnison, M.B., B.Chir., Assistant Resident Medical Officer, Tadworth Court; Barbara G. Ockenden, M.B., B.S., Assistant Morbid Anatomist; G. C. Lloyd-Roberts, M.B., F.R.C.S., Part-time Consultant Orthopaedic Surgeon; Dragomir Vuckovic, House-physician to Neurological and Neurosurgical Department; J. A. Cheese, M.D., D.C.H., and Rosemary Stephens, M.B., B.S., D.C.H., House-physicians; F. N. Bamford, M.B., Ch.B., House-surgeon.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Abraham.—On March 12, 1955, at the Bristol Maternity Hospital, to Beryl (formerly May), wife of Dr. Ross Abraham, a sister for Lindsay—Susan Diane.

Bird.—On March 11, 1955, at the Jessop Hospital for Women, Sheffield, Yorks, to Nora (formerly Bateman), wife of Dr. Julian Bird, a daughter.

Carstairs.—On March 5, 1955, to Jean (formerly Dutton), wife of Captain J. R. L. Carstairs, R.A.M.C., British Military Hospital, Up Park Camp, Kingston, Jamaica, British West Indies, a son—Andrew James.

Herdman.—On March 14, at Crickhowell, Brecs, to Betty Howarth, M.B., M.R.C.P., wife of G. J. S. Herdman, M.B., a daughter.

Roche.—On March 4, 1955, at St. Teresa's Maternity Hospital, Wimbledon, London, S.W., to Susan (formerly Margaret), wife of Dr. G. K. T. Roche, a brother for Patricia, Peter, and Stephen.

DEATHS

Holker.—On February 25, 1955, at Withington, Glos, John Holker, M.D., D.Sc., late of Manchester, and Florida, U.S.A.

Hyslop.—On February 23, 1955, at Newcastle-upon-Tyne, Vincent Hyslop, M.R.C.S., L.R.C.P., of Newcastle, and 3, Prince Edward Mansions, London, W., aged 61.

Low.—On March 4, 1955, at Muirlands, Larbert, Stirlingshire, Natan Chaim Low, M.D., aged 43.

Macdonald.—On February 10, 1955, in a nursing-home, Chrisslebelle Macdonald, M.B., Ch.B., of "Dornoch," Golborne, near Warrington, Lancs.

Macpherson.—On March 3, 1955, at 9, Bellevue Crescent, Edinburgh, Alexander Macpherson, M.B., Ch.B., late of Accra, Gold Coast.

Martin.—On February 20, 1955, at Weston-super-Mare, Somerset, Philip Stanley Martin, *M.C.*, M.R.C.S., L.R.C.P., aged 69.

Moorhead.—On February 26, 1955, at "Nantai," Tower Road, Jersey, C.I., John Moorhead, L.R.C.P.&S.Ed., L.R.F.P.S., aged 88.

Nuttall.—On February 19, 1955, at Rivermead, Rickmansworth, Herts, Arthur Peel Nuttall, M.D., late of Bury, Lancs, aged 85.

Palmer.—On February 26, 1955, at his home, 14, Windlesham Road, Brighton, Charles Spencer Palmer, M.R.C.S., L.R.C.P., late of Redhill, and Torquay, aged 88.

Parsons.—On March 4, 1955, at Kirkcudbright, Wilfred Parsons, M.R.C.S., L.R.C.P., Major, R.A.M.C., retired, of Colchester, Essex, aged 76.

Powell.—On February 27, 1955, at Pemberton House, Hay, Hereford, Hubert Wybrants Powell, L.R.C.P.&S.Ed., L.R.F.P.S., formerly of Passage West, Co. Cork.

Reed.—On February 20, 1955, at The Vicarage, Westbury-on-Trym, Bristol, William Henry Reed, L.M.S.S.A., formerly of Charlton, London, S.E., aged 90.

Russ.—On February 26, 1955, Charles Russ, M.B., of 7, Carlton Road, Ealing, London, W.

Scruby.—On March 2, 1955, Zilla Mary Scruby, M.B., B.S., D.P.H., of "Corrie," 21, Newton Road, Cambridge.

Shipsey.—On March 4, 1955, at Hospital of St. John and St. Elizabeth, London, N.W., William Edward Shipsey, L.R.C.P.&S.I. & L.M., of Beckenham, Kent.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Breads for Diabetics

Q.—*Which of the various kinds of special breads is best for diabetics?*

A.—There is not a great deal of difference between the carbohydrate values of the various proprietary diabetic breads. They vary from about 10 to 14 g. of carbohydrate per ounce (28 g.) compared with about 12.5 g. for wholemeal and 15.2 g. for white bread. The chief advantage of the special breads is that they are lighter in texture so that a greater bulk goes to the ounce. For example, four slices of one brand of diabetic loaf contain about 10 g. of carbohydrate, which is the same as one small slice of ordinary bread. The choice of bread for any individual diabetic is a matter of taste, but it should be realized that whichever bread is used the actual weight eaten for a given carbohydrate intake will not vary much, although the size of the slices may.

Head Lice

Q.—*What is the most effective (a) prophylactic and (b) curative treatment for a girl, aged 7, who is being constantly reinfected at school by other children harbouring head lice? The child is clean, from a good home, and well cared for.*

A.—It is not definitely known how, or to what extent, lice spread among children at school. One possibility is the use of communal hair brushes and combs, and if they are provided by the school in question the girl should be told not to use them. A short and easily combed hair style might be adopted as being less liable to become infested.

The best treatment for head lice is a thorough combing with a fine-toothed metal comb (a "Sacker" comb) to remove nits, followed by the application of an efficient insecticide. One of the best is 0.2% aqueous suspension of gammabenzene hexachloride (lindane); 2% dicophane (D.D.T.) emulsion is nearly as good. About 5–15 ml. is applied and rubbed in. The insecticide is imperceptible and should not be washed off for a week, when a further treatment is applied after a shampoo.

These insecticides could be applied regularly as prophylactics, though it is unfortunate that this should be necessary. If the girl's medical adviser is convinced that school is the source of the trouble, he might bring the matter to the attention of the school medical officer.

Prognosis and Treatment of Asthma in Children

Q.—*May I seek your advice on the prognosis of asthmatic bronchitis in children and its treatment? My son, 3 years old, started the attacks a year ago after whooping-cough. The attack begins with coryza, then cough, and within a day or two wheezing and dyspnoea develop. He is also subject to urticaria. As the attack progresses the respiratory rate drops slowly to reach normal within two days. Chest radiography showed increased hilar shadow.*

A.—The prognosis of asthmatic bronchitis in children is good, especially so under favourable environmental circumstances. Collins[1] in the United States has shown that the annual case rate for asthma decreases from 3.3 per 1,000 in the under 5 years of age to 0.7 per 1,000 in the age group 15–19 years (based on records of 9,000 families in 18 States visited periodically for twelve months).

Prophylactic treatment is based on reducing the tendency to nasopharyngeal and chest infection. Adequate sleep, avoidance of excessive excitement and over-tiredness, adequate vitamins, prevention of chilling by correct clothing and warmth in the bedroom in the colder months, together with the avoidance of transference of colds from other members of the family by correct hygiene are basic requirements. It is unlikely for there to be any focus of infection in the upper respiratory tract at the age of 3 years, but the advice of an E.N.T. specialist might be obtained. Vaccines are of doubtful value. Prophylactic antibiotic therapy is perhaps best left as a last resort until all other measures have failed, and one should bear in mind the natural tendency to improve. The possibility of extrinsic allergens, foods and inhalants, playing a subsidiary or even occasionally precipitating part must be considered, especially in a child with urticaria; nor should the psychological factor be overlooked.

The treatment of the attack should start at the onset of the coryza, when there is presumably a temperature, with warmth and plenty of fluids and glucose. Antibiotics (preferably by mouth) should be given early on, at least as soon as the cough develops, and continued until the attack and temperature have ceased. The usual treatment with ephedrine and expectorants, to relieve spasm and liquefy the sputum, should also be started as soon as the cough and wheeze occur.

REFERENCE

[1] Collins, S. D. (1935). *Publ. Hlth Rep. (Wash.)*, **50**, 1404.

Sterilizing Infected Laundry

Q.—*As an economy measure all laundry from a fever hospital is in future to be sent to a communal laundry for hospitals in the group. Prior to dispatch it must be "suitably sterilized." What method is recommended? One view is that a formalin candle would be sufficient.*

A.—The procedure advised in the Medical Research Council Memorandum *The Control of Cross Infection in Hospitals* (Memorandum No. 11, 1951) is soaking overnight in a 1 in 160 solution of an efficient disinfectant of the "white fluid" type. Exposure to a low concentration of formaldehyde at room temperature, besides being more difficult to provide for, would probably fail to disinfect heavily soiled linen.

Fertility in Unilateral Cryptorchidism

Q.—*A man of 35 with one undescended testicle, untreated, wishes to marry. The penis, the testicle present, and the secondary sexual characteristics appear normal. He has never had intercourse, but experiences desire and has had erections. His general health and development are satisfactory. Is he likely to be normally potent, and what is the prognosis as regards fertility? Is any treatment or investigation recommended? He is one of four children, and his fiancée comes from a fairly fertile family.*

A.—From the information given, there seems no reason to doubt that this man would be normally potent, but the prognosis as regards fertility is less certain. If, in fact, the scrotal testis is normal, then he should be normally fertile, but it is a matter of experience that the scrotal testis in a case of unilateral cryptorchidism is often dysplastic to a varying extent even though it may always have been fully descended.

On the whole I would advise against investigation at this stage, since the decision to marry should not be contingent upon the certainty of fertility. If, however, the patient has other views, then of course a seminal analysis should settle the point.

"Ronicol"

Q.—*Can you please tell me what are the dangers of, and contraindication to, giving "ronicol" a trial in the treatment of baldness?*

A.—"Ronicol" (β-pyridyl carbinol) has a dilating effect upon the small arteries and arterioles. This lowers the peripheral vascular resistance and tends to lower the blood pressure. Large doses may therefore produce giddiness, faintness, or vasovagal attacks. The dosage should be small to start with and later increased, provided no

signs of intolerance are shown. It is usual to start with 25 mg. orally four-hourly and later increase it to 50 mg.

There are no particular contraindications to the use of this drug in otherwise healthy individuals, but it would be unwise to take the drug immediately before a hot bath, as the risk of a vasovagal attack would then be greater.

The observation that a good crop of hair grew on the bald scalps of two patients under treatment with ronicol for intermittent claudication[1] does not seem to have been repeated. Had the beneficial effect of this drug on baldness been established there would be no lack of reports about it, and it seems reasonable to suppose, therefore, that the growth of hair must have been coincidental.

REFERENCE

[1] *British Medical Journal*, 1954, **2**, 648.

Electrical Alternation in the E.C.G.

Q.—*What is the significance of electrical alternation seen in the E.C.G.? Can it occur as an isolated phenomenon, and, if so, what significance does it then have?*

A.—This is a fatigue phenomenon and probably means that not all the myocardium can respond every time to each stimulus. It is not uncommon with very fast rates, but occurring with slower rates it means myocardial disease. It is unlikely to be met with as an isolated phenomenon.

Treatment of Cyclical Agranulocytosis

Q.—*Is there any known treatment which is effective for cyclical agranulocytosis? The condition has been present for 18 months in a boy of 8. Splenectomy has been considered, but in view of its uncertainty postponed. The matter is one of urgency, as the child's life is endangered during each incident of neutropenia, in some of which the granulocyte count falls to nil.*

A.—There is no effective specific treatment for cyclical agranulocytosis, so far as the writer knows. A.C.T.H. has been used in several patients, but does not seem to be of benefit.[1] However, according to Reimann and de Berardinis,[2] who reviewed 16 cases, splenectomy produced amelioration of the symptoms or in the severity of the neutropenia in four out of six patients. There also appears to be a possibility of spontaneous improvement, and, if it is decided not to proceed with splenectomy, palliative treatment with antibiotics to cover the periods of agranulocytosis seems to be the best that can be done.

REFERENCES

[1] Chaiken, B. H. (1954). *Blood*, **9**, 83.
[2] Reimann, H. A., and de Berardinis, C. T. (1949). Ibid., **4**, 1109.

NOTES AND COMMENTS

Oversexed Women.—Dr. MARGUERITE STEWART (London, S.W.4) writes: The reply in "Any Questions?" on oversexed women (February 26, p. 553) is deeply disturbing. It shows the wide cleavage between the materialistic and the Christian approach. To support masturbation as the answer is defeatist, leaving the person feeling degraded at being encouraged to regard a standard of behaviour which she feels less than the highest as adequate for her. In over 25 years of handling of every type of human problem in general practice, I have seen that the miracle of change and victory is possible. This needs to be stated.

Dr. J. KOHARI (London, S.E.11) writes: I was perturbed to note the ignorance of your expert on the problem of the oversexed woman ("Any Questions?" February 26, p. 553). After treating the patient with phenobarbitone and ethisterone he indulged in the praise of masturbation, using the Kinsey report as an authority. Does he suggest this as medical advice, or, if not, why mention it? This is a straightforward example of crooked thinking, because masturbation is connected with sexual stimulation and it is the sexual excitement that we want to cure. The breathlessness of those with congestive cardiac failure is not treated with climbing stairs, or the heartburn of those with peptic ulceration is not treated with irritating spices. Further, let us have the facts right. I would be interested to know whether the 96% of males or 60% of females who in the Kinsey report are said to masturbate applies to those who continuously indulge in this procedure throughout life or do so for a short period, perhaps during puberty while they actually discover the function of their own body. The oversexed woman cannot be treated with tablets alone without regard to the background of her life. I refer to the reading of stories obsessed with sex and the viewing of similar motion-pictures. I do not wish to be misunderstood. I do not wish to limit anyone in these entertainments, but if my professional advice is sought on the treatment of sexual hyperexcitability then I should advise against them. Nor is this all. This is the negative side of the question. The patient should be told to find other activities—for example, sports, hobbies, social work, etc.—which will divert her mind and sap her unlimited energies. Also it is not a bad idea to have children, as they will probably provide an object for her adoration and an additional outlet for her trouble.

Dr. J. W. DIGNAN (London, E.7) writes: It is regrettable that the note on oversexed women (February 26, p. 553) should, in a medical journal, occupy itself with morals and should proclaim masturbation to be a normal activity free from moral or psychological stigma. One cannot but be startled by the assertion that "such advice would probably be given by most present-day psychiatrists." Surely psychology ranks masturbation as a symptom of an immature personality.

OUR EXPERT writes: I am sorry that my brief comment on masturbation in oversexed women should have caused offence to some readers. My reply was designed for doctors. It seemed reasonable, therefore, to dismiss quite shortly the obvious, time-honoured advice—which Dr. Kohari rightly stresses—by my sentence, "Sensible advice about behaviour, masturbation, and the avoidance of alcohol would doubtless also help." Indeed, every doctor must know that one advises "sports, hobbies, and social work" to men or women who suffer from sexual strain; and for married women childbearing is normally the best solution.

I assumed from the wording of the question that it related to unmarried women, and anyone who advises students and young people will know how, in some cases, the degree of effort needed to suppress sexual tension may be so great as to become in itself almost a whole-time task. For such a person I suggested that it might be better to accept the natural relief of masturbation rather than to be obsessed by a physiological tension which self-discipline, overwork, and over-exercise cannot really suppress. In Victorian times the condemnation of self-relief reached, in this country, fantastic levels: the young were threatened with insanity, impotence, and so on if they indulged in it. Surely thoughtful people nowadays take a more rational attitude. It is often possible for the doctor to give infinite relief by reassuring a patient that this practice will not have damaged his or her future marital capacities.

Dr. Dignan misrepresents what I wrote. I did not state that masturbation is "free from moral and psychological stigma," but I suggested that it might be considered "normal in the celibate adult," although "admittedly the question is a complex one." Dr. Dignan implies that there are absolute standards in matters of psychological maturity: a point of view with which I should not, personally, agree. If a married person prefers masturbation to sexual congress, one would obviously diagnose a condition of psycho-sexual immaturity. But situations differ. Troops when overseas and away from their wives quite often resort to masturbation in preference to infidelity, and that surely does not brand them as immature personalities.

Correction.—Dr. M. I. Drury's address at the foot of his letter on isophane insulin (*Journal*, March 19, p. 730) should have been given as Dublin, not Sunderland.

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